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The Royal London

Ophthalmic Hospital Reports.

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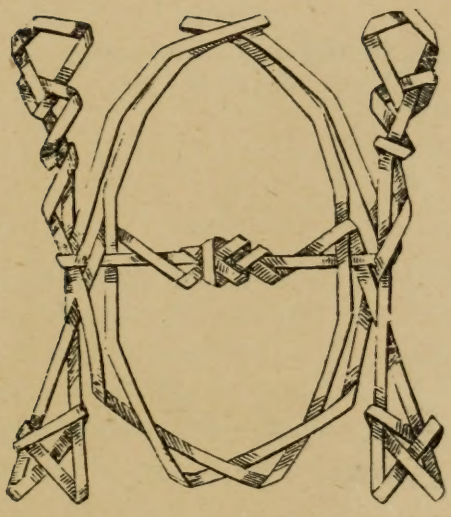

VOLUME SIXTEEN.

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The Royal London

Ophthalmic Hospital Reports.

VOL. XVI. PART I. JUNE, 1904.

I. ON RENAL RETINITIS IN YOUNG SUBJECTS AND ON THE RELATIVE FREQUENCY OF JUVENILE INTERSTITIAL NEPHRITIS IN THE TWO SEXES.

By E. NETTLESHIP.

IN a paper upon the ocular changes that occur in renal disease in vol. xv, Part IV of these Reports, a short statement was made as to albuminuric retinitis in children and young subjects. The scanty data I had then had the opportunity of collecting suggested that the subject, if followed up, might reveal points that would be of interest to physicians in their researches upon chronic nephritis in children, and especially the interstitial forms of that disease.

Owing to the kindness of the staff of the Hospital for Sick Children, Great Ormond Street, I have been able to search the in-patient and *post-mortem* books of that Institution from 1864 to 1903, and have obtained much valuable material. My best thanks are also due to Dr. H. P. Hawkins, Dr. Leonard Guthrie, Dr. George A. Sutherland, Dr. J. E. H. Sawyer, Dr. George Carpenter, Dr. Miles Miley, and others, for information, and for leave to make use of cases. I am especially indebted to Dr. J. E. H. Sawyer's elaborate paper on "Chronic Interstitial Nephritis in Children,"* published

* J. E. H. Sawyer, The Birmingham Medical Review, August and September, 1903.

almost at the same time as my paper on renal retinitis above mentioned, for references to additional cases. I have also found some published cases not referred to by any of the above writers. Some of Dr. Sawyer's cases were obtained, like some of mine, from the Hospital for Sick Children, but I have taken care not to count any of these twice.

From the above-mentioned, and various other, sources, just 80 cases of interstitial nephritis* in patients not more than 21 years of age have been collected, including 9 cases of my own given in greater or less detail in the paper already referred to. In addition, I have found 3 cases in which the chronic nephritis was associated with calculus in kidney or bladder: if we counted these the total would be 83.

Of the total number the date of death is known in 62, and in 60 a *post-mortem* examination was made. In the remainder the issue was not fatal, or the date of death could not be ascertained, and in reckoning these as examples of granular or interstitial nephritis I have been guided by the recorded diagnosis, or, when the written heading to an unpublished case was inconclusive, I have taken the evidence afforded by the notes.

This collection of cases of granular or interstitial nephritis is obviously by no means uniform. The want of homogeneity is owing, no doubt, in a few instances to mistakes in my choice of cases, but much more to the fact that death does not always occur at the same stage of the kidney disease, and possibly to the inclusion, unavoidable at present, of more than one pathological species. Upon such pathological points I am not competent to speak; but it is clear from published cases that, *e.g.*, the natural history of the acute interstitial nephritis of infants has not yet been fully worked out, and that its relation to the extreme forms of granular contracted kidney from which elder children

* I have made no attempt to separate the "true granular contracted" from the "small white" kidney; and I have included cases of early nterstitial nephritis.

occasionally suffer is at the present time more a matter of inference than proof.

But whatever subdivisions it might be possible to make in the 80 cases that I have classed as interstitial nephritis, that group can certainly, as a whole, be separated clearly from the parenchymatous series. Keeping the two classes distinct, I have tried in what follows to ascertain, without going beyond what may be included within the ophthalmologist's purview, whether anything can be made out by a comparison between them that may throw light upon the etiology of interstitial nephritis in children.

For purposes of comparison I have, therefore, examined the notes of all the cases diagnosed as parenchymatous nephritis, or inferred from the notes to be of that nature, at the Hospital for Sick Children,* omitting all very recent cases of scarlatinal nephritis, and also the cases (7 in number) of well-marked amyloid disease. In this way a series of 149 cases has been obtained. Fifty-six of these were fatal, and in 50 a *post-mortem* examination was made.

Retinitis, or multiple retinal hæmorrhage, was observed in 31 of the 80 cases of interstitial nephritis, and in 2 out of the 3 examples of granular or contracted kidney associated with calculus. The eyes were examined, and found normal in about 10 others. In the remainder (about 37) no ophthalmoscopic examination seems to have been made.

Amongst the 149 parenchymatous cases definite retinitis was found in 7, and doubtful appearances—such as slight haziness of the discs—of uncertain significance, in several more. In about 43 the eyes were examined and found normal, and in the remaining 90 there was apparently no ophthalmoscopic examination.

In the 7 cases of amyloid disease the ophthalmoscope seems to have been used to only 1, and in that 1 the fundi were normal.

* Increased by some 20 to 30 cases published or communicated by Dr. Miles Miley and others.

Amongst the total number of 40 cases of retinitis in both groups, the number in which the eye changes were very severe was larger than in any similar consecutive number of cases in older subjects. Both retinæ were detached in 3 patients, very abundant hæmorrhage formed a marked feature in 2 or 3 others, whilst the exudation and swelling were excessive in 3 or 4 more. But we must not hastily conclude from this result that the ocular changes are especially liable to reach an unusually high degree in the young; for it is likely enough that milder degrees of retinitis causing little interference with sight would have been discovered in a good many more of the children had the ophthalmoscope been used by routine.

A similar remark applies to the apparent scarcity of retinal changes in parenchymatous as compared with interstitial nephritis in the young—the ophthalmoscope was used much less frequently in the parenchymatous cases than in the others.

The earliest age at which renal retinitis has been recorded seems to be 5 years (Bull's case, a girl).* Amongst 40 cases (interstitial and parenchymatous) I find 2 cases æt. 7 years, 3 of 8 years, 2 of about 9, 3 of 10, 2 of 11, 5 of 12, or in all about 18 below the age of 13 years. Rather more than half of the series (23 cases) were æt. from 14 to 21 years. Twenty-six of the whole number were females, 14 males.

Of these 40 young patients with retinitis, 24 died at a known interval after the eye condition was first discovered This interval was $3\frac{1}{2}$ years in 1 case,† between 12 and 15 months in 4 cases, between 4 and 7 months in 3 cases, and less than 4 months in 16 cases.

From the data at present available it appears, therefore, that the prognostic importance of the retinal changes in chronic renal disease is certainly not less grave, perhaps

* Two cases at the Great Ormond Street Hospital, æt. 4 and 5 years respectively, showed slight questionable appearances of neuro-retinitis.

† Case of Theresa R. in my previous paper, p. 330.—E. N.

more so, in children and young subjects than it has long been known to be in adults.*

In my previous paper I found that chronic renal disease occurring below the age of 21 was commoner in females than males, exactly the reverse of the rule obtaining for older subjects; but the number of cases then counted was too small to allow of any but a provisional conclusion on such a point. The same fact, an excess of females over males, was also observed by Sawyer and was remarked upon by Handford as long ago as 1890. On examining the entire series of 80 cases this conclusion is strongly confirmed, the females being to the males as 51 to 28,† (64 and 36 per cent.) or nearly twice as many females as males.

In order to ascertain whether the relative frequency of the sexes is the same in the parenchymatous as in the interstitial disease we must compare cases of the same age in each series. This I can do by taking only those of both kinds, interstitial and parenchymatous, below, say, 13 years of age, that being about the maximum age allowed at the children's hospitals. My parenchymatous series below the age of 13, consists of 130 cases; of this number 70 are males (54 per cent.), and 60 females (46 per cent.), a slight but decided excess of males. Dickinson using partly the same material, found nearly the same proportions. Of the entire interstitial nephritis series, 51 patients were less than 13 years old, and of these 16 (about 30 per cent.) were males and 35 (nearly 70 per cent.) females, an even larger excess of females than is found when the cases aged from 13 to 21 years are included. Though these numbers are comparatively small they confirm the earlier provisional conclusion arrived at by Sawyer and myself, *viz.*, that interstitial nephritis in the young is much more frequent in females than males. They show further that the same does

* See Marcus Gunn, Trans. of Ophth. Soc.; Miles Miley, *ibid.*; Bull and others.

† In the remaining case the sex is not mentioned.

not hold good in parenchymatous nephritis at the corresponding ages, where the males are slightly in excess.

It would be easy for anyone, who could give the necessary time, to examine a much larger number of cases of parenchymatous nephritis in young persons, and confirm or refute my finding as regards the sex liability in this class, for parenchymatous nephritis is sufficiently common in children. In the meantime we may note that, whilst the figures given above show that there is some excess of males over females in children suffering from this form of chronic nephritis, the inequality is much less than in adults.*

This marked excess of females over males in the interstitial cases in young subjects, contrasting as it does so strongly with the excess of males in adults suffering from the same form of disease, and the greater or less excess of males in both adults and children in the parenchymatous forms, is certainly very striking. The explanation of such an unexpected fact must be left for future research. The reason certainly cannot be found in the greater exposure to weather, lead poisoning and alcohol of the more affected (*i.e.*, female) sex; and apparently not in any special influence of puberty in the female, since the preponderance of females over males seems, as already stated, to be less between the ages of 13 and 21 than it is below the age of 13 years.†

Can a partial explanation be found in a corresponding excess of girls over boys born syphilitic and surviving early infancy ?‡, or in differences of frequency or character in scarlet fever as it affects the two sexes ?§

* In adults, according to Dickinson, tubal and diffuse nephritis is more than twice as frequent in males than in females.

† I have 27 cases of interstitial nephritis in patients æt. from 13 to 21, and of these 15 were females, 12 males.

‡ In respect to sex in the subjects of inherited syphilis, Hutchinson states, in his classical monograph (1863), that of 102 patients with interstitial keratitis, 64 were females and 38 males, or about 63 and 37 per cent. respectively.

In 564 consecutive cases of the same eye malady, I find 339 females and 225 males, or 60 and 40 per cent. respectively.

§ In regard to scarlet fever, Dickinson, in discussing the reasons for the

The view that congenital syphilis is often the cause of acute infantile nephritis, usually interstitial, appears to be gaining ground. Future observations may be expected to decide the question whether, when such infants survive, they sometimes die in their teens from advanced granular kidney disease, and also, if this be so, whether they generally show the common dental and facial sign of hereditary syphilis? Very little is to be found in the notes of cases of juvenile granular kidney as to the condition of the permanent teeth or the physiognomy, a piece of negative evidence that I think cannot be entirely accounted for by defective note-taking.

It may save trouble to future workers if I take out the facts as to scarlet fever and some other reputed causes of granular kidney in children now that the records of a number of cases are before me. In upwards of 30 of the 80 cases the notes of previous history at my disposal were incomplete, leaving about 45 for use in this connection.

Scarlet fever is stated to have occurred before renal symptoms began, in 16 of these 45 cases from the granular kidney series (13 girls, 3 boys) the interval between the fever and the recognised renal symptoms being never less than about 2 years, and often much more. In at least 6 cases scarlet fever was definitely denied.

Measles alone, or with the added effect of chicken-pox, was assigned as, or seemed to be, the most probable cause in about 8 cases.

In 1 case there was a history of an unnamed fever; in 2, severe prolonged infantile eczema;* in 2, severe infantile diarrhœa; in 1 or 2 rickets, arrest of growth and subsequent failure of intelligence. In 3 cases there was a clear history

excess of males over females in chronic nephritis as a whole, and also in fatal scarlatinal dropsy, adds "it is to be observed at the same time that the deaths from scarlatina are nearly the same for both sexes." "Diseases of the Kidney and Urinary Derangements," Part II, pp. 267 and 321 (1877).

* Eczema also appeared to be the cause in 2 of the parenchymatous cases.

of stone in the kidney and bladder. In 3 cases alcohol was presumably the cause, 2 being lads who drank heavily, 1 a young barmaid who owned to taking neat brandy before breakfast and was a large meat eater.

Hereditary syphilis was proved in only 6 cases of interstitial nephritis, 3 of these being infants; but it was highly probable in several others. It was certainly the cause in 4 of the parenchymatous cases. This rather meagre record of facts, in contradistinction to opinion as regards congenital syphilis, points to the need for much more careful inquiries in future.

In several of the 45 granular cases all history of previous illnesses was denied, but a history was given of polyuria and thirst dating from early infancy.

From the above it seems that one or another of the specific fevers, including syphilis amongst them, might be assigned as the cause of interstitial nephritis of children in at least 31 out of 45 cases, whilst some other profound disturbance of infantile health had preceded the appearance of renal symptoms in several others.

It appears that the same specific fevers may be claimed with something like the same frequency as the cause of parenchymatous nephritis in young subjects, *e.g.*, in at least 45 of 150 cases, a proportion representing, however, much less than the whole truth, since the clinical history at my disposal was even more frequently incomplete in the parenchymatous than the interstitial cases.

References to the Cases of Chronic Nephritis in Young Subjects.

1. 1864. Hulke. Roy. Lond. Ophth. Hosp. Reports, vol. v, p. 20. — 1 case.
2. 1871. Hutchinson. The Lancet, vol. i, p. 479 .. 1 „
3. 1873. Jabez Hogg. The Lancet, vol. ii, p. 701 .. 1 „
4. 1873. Magnus. Albuminurie in Ihre Ophthalmoscopischer Erscheinungen. — 2 cases.
5. 1874. W. H. Barlow. The Lancet, vol. ii, pp. 151, 192 — 1 case.

6.	1877.	DICKINSON. "Diseases of the Kidney and Urinary Derangements," Part II, Albuminuria, pp. 376 and 427; 4 cases, 1 of which (A. R., æt. 10) is republished by Sawyer as his Case 3 (see below).	4 cases.
7.	1872.	GULL and SUTTON. Medico-Chirurg. Trans., vol. lv, p. 301.	1 case.
8.	1879.	GOWERS. Medical Ophthalmoscopy, p. 302 ..	1 ,,
9.	1883.	ARTHUR H. BENSON. Trans. of the Academy of Medicine, Ireland.	1 ,,
10.	1886.	C. STEDMAN BULL. Trans. of American Ophthalmological Society, vol. iv, p. 184.	1 ,,
11.	1888.	JAMES ANDERSON. Trans. Ophthalmological Society of United Kingdom, vol. viii, p. 141.	1 ,,
12.	1888.	MILES MILEY. *Ibid.*, p. 135	2 cases.
13.	1889.	GEORGE CARPENTER. "Syphilis of Children in Everyday Practice." Repeated in Reps. Soc. Study of Disease in Children, vol. iii, p. 287 (1903).	1 case.
14.	1889.	HENOCH. Lectures on Diseases of Children, vol. ii. (New Sydenham Society).	1 ,,
15.	1890.	H. HANDFORD. Trans. Pathological Soc. of London, vol. xli, p. 165	1 ,,
16.	1890.	HALE WHITE. *Ibid*	1 ,,
17.	1890.	W. J. COLLINS. Trans. Ophthalmological Soc., United Kingdom, vol. x, p. 148.	1 ,,
18.	1890.	GOODHART. Keating's Cyclop., "Diseases of Children," vol. iii.	5 cases.
18*a*.	1894.	MASSALANGO. Medical Record, p. 534.. ..	1 case.
19.	1895.	BEAUMONT. British Med. Jour., vol. i, (April 20)	1 ,,
20.	1897.	EMMETT HOLT. Archives of Pediatrics, vol. iv, p. 1 (23 cases of primary nephritis in infants). Of these 23 cases I have only used 6, viz., those in which the sex is given and a *post-mortem* examination was made. Of the 6, 3 were interstitial, 3 parenchymatous.	
21.	1897.	LEONARD GUTHRIE. The Lancet, vol. 1, February 27 and March 13, and Reports of Society for Study of Disease in Children, vol. i (January 18, 1901).	1 ,,
22.	1898.	HOLMES SPICER. Trans. Ophth. Soc., United Kingdom, vol. xviii, p. 145.	1 ,,
23.	1899.	HOLMES SPICER. *Ibid.*, vol. xix, p. 73.. ..	1 ,,
24.	1898–99.	SUTHERLAND and LAWSON. *Ibid.*, vol. xviii, p. 140, and vol. 19, p. 71.	1 ,,
25.	1899.	A. E. RUSSELL. St. Thomas's Hospital Reports, vol. xxviii, p. 63.	2 cases.
26.	1899.	GOODHART. Ashby and Wright's Diseases of Children, 4th ed.	

27.	1900.	J. B. Lawford. Norris and Oliver's Handbook of Ophthalmology, vol. iv, p. 652.	1 case.
28.	1901.	Sequeira. Reps. Soc. Study of Disease in Children, vol. i, p. 17.	1 ,,
29.	1902.	Milligan. *Ibid.*, vol. ii, p. 99	1 ,,
30.	1902.	Sydney Stephenson. *Ibid.*	1 ,,
31.	1902.	Carpenter. *Ibid.*	1 ,,
32.	1901.	Schmidt-Rimpler. Graefe-Saemisch Handbuch, Kap. xxii, p. 98.	1 ,,
33.	1901.	Groenouw. *Ibid.*, p. 99..	1 ,,
34.	1903.	Carpenter. Reps. Soc. Study of Disease in Children, vol. iii, p. 287 (1 new case, in addition to Reference 13 above).	1 ,,
35.	1903.	Jas. E. H. Sawyer. Birmingham Medical Review, August and September.	5 cases.
36.	1903.	Nettleship. Roy. Lond. Ophth. Hosp. Reports, vol. xv.	10 ,, (6 given in detail).
37.	1903.	Sutherland and Walker. Reps. Soc. Study of Disease in Children, vol. iii, p. 134.	2 cases.
38.		Bartels. Ziemssen's Cyclop. Practical Medicine, vol. xv, p. 426.	1 case.
39.	1898.	Filatoff. Mal. de L'enfance Trans. by Perier. Male, æt. 12. Typical changes, *post-mortem*.	1 ,,

Unpublished cases have been kindly communicated by—

Dr. H. P. Hawkins	..	1 new case.
Dr. G. A. Sutherland	..	2 new cases.
Dr. Jas. E. H. Sawyer	..	4 new cases from Guy's Hospital and the Queen's Hospital, Birmingham.

The staff of the Hospital for Sick Children, Great Ormond Street :— 15 cases of granular disease of the kidney in children. Of these cases 10 are new, and 5 have been already published, viz., 2 by Dr. Dickinson, 1 by Sir Thomas Barlow and Dr. Judson Bury, and 2 by Dr. Jas. E. H. Sawyer.

Additional particulars as to certain of the published cases have been added through the kindness of—

Sir W. J. Collins.
Dr. Colman.
Dr. Miles Miley.
Mr. Hartridge.
Dr. Jas. E. H. Sawyer.
Dr. C. Stedman Bull.

II. OBSERVATIONS ON THE PROGNOSTIC AND DIAGNOSTIC VALUE OF RETINITIS IN DIABETES.

In a previous paper, already referred to, I mentioned my belief that the presence of retinal changes in a person with diabetes does not point to the probability of early death with the same frequency as does the retinitis of chronic Bright's disease, and I feel sure that others must have had a similar experience.

I am now able, owing chiefly to the courtesy of numerous medical friends, to give some particulars of the duration of life and mode of death in 48 patients with diabetic retinitis, or retinal hæmorrhage, who have been under my care.

The age of these patients ranged from 41 to 79 years. Of the 48 patients, 38 are known to have died. Of this number 9 died within 12 months of the discovery of retinitis or the failure of sight caused by it,* and 11 others during the second year, *i.e.*, 19 died within 2 years of the retinitis being discovered. The remaining 18 died at periods varying between 2 and 8 years, and to this number must be added 10 others, who are known to be, or have been, living at dates varying from 2 to 10 years from the retinitis.†

Thus we find that of the 48 cases no less than 28, or nearly two-thirds, or exactly 60 per cent., lived more than 2 years after the eye disease was found, and only 9, or about one-fifth, died within one year. This is very widely different from the history of ordinary renal retinitis (excluding pregnancy cases), in which I find that in my own cases less than one-third lived 2 years after the retinitis and nearly two-thirds succumbed within 12 months.

* The date of commencement of the fundal changes can seldom be fixed, especially as in these elderly subjects there is often some slowly forming opacity of the lens. But in a few instances the retinitis could be dated with tolerable precision.

† Six of these are now living from 6 to 10 years from my first examination.

The prognosis for life is, therefore, clearly much better in the diabetic cases of all ages than in the renal cases of all ages (excluding those caused by pregnancy).

The great majority of the subjects of diabetic retinal changes are more than 50 when the eye changes occur, and in order to compare the relative significance of the retinitis in this malady and in Bright's disease, cases at the same time of life must be chosen. Such a comparison shows that the relatively more fatal significance of albuminuric retinitis holds as decidedly for the more senile group as for the entire class, and the longer average duration of life in diabetic retinitis must, therefore, be ascribed to the different nature of the two principal maladies rather than, as I tentatively concluded in the earlier communication, to some influence of age as such.* Indeed, the figures indicate that in the diabetic group the prospect of life is certainly not better, but probably rather worse, if the retinitis occurs after 55 than before.

The character of the ocular changes is much less uniform in diabetes than in chronic nephritis, and consequently the diagnosis of diabetes or glycosuria from the presence of retinitis or retinal and vitreous hæmorrhages cannot be made with the same near approach to certainty as it can be from the retinal changes in Bright's disease. In spite of their variability the changes observed in the cases of diabetes are, however, of much assistance in diagnosis, especially in the diabetes of elderly and old persons, in which the general symptoms are often mild, and may easily be overlooked.

The disease of retina, due to diabetes, seems, one may almost say, to be a more local affair than it is in renal disease, for we find that in many of the diabetic cases the retinal degeneration (exudation and hæmorrhage) increases either steadily, or by repeated relapses, even when the general condition of the patient has improved and is

* Of 24 patients, æt. 55 and upwards, with renal retinitis, exactly one-third survived for 2 years. Of 38 with diabetic retinitis, æt. 55 and upwards, rather more than half lived 2 years or more.

continuing to be satisfactory. As regards improvement of vision, therefore, the prognosis in diabetic retinitis should be very guarded.

As examples, the following may be mentioned:—

CASE 14.*—A gentleman, aged 56 when first seen, has now, 10 years later, become nearly blind. He underwent amputation of the leg above the knee for gangrene of the foot with success a year ago, *i.e.*, when he was 65.

CASE 23.—A lady, aged 47, with retinitis and diabetes, lived 8 years afterwards, dying of diabetic coma when 55. Her sight got worse, and she was blind before she died.

CASE 19.—A gentleman, aged 47 when first seen, suffered repeated relapses of large hæmorrhage from retinal vessels, the vitreous finally becoming almost opaque before he died at the age of 50.

CASE 43.—A diabetic lady, whose sight began to fail from retinal, chiefly vascular, changes when she was 45, is now about 52 and in what is called excellent health, but absolutely blind.

Half a dozen other instances could be given in which the vision of patients who lived several years deteriorated more or less before death.

On the other hand, cases can be cited in which vision has kept nearly stationary:—

Case 40 is that of a lady whose retinal mischief occurred when she was about 63; she knew that she could control her malady by careful living, but told me she "would rather die of it than give up the things she liked." She is still living, aged about 67, and her sight, though rather worse, still allows her to read what she wants of the newspaper. She still has glycosuria.

CASE 48.—A gentleman, whose sight failed from diabetic retinitis when he was 67, is now 74 and his vision no worse.

* In my series.

Case 12 is that of a cashier in a bank, whose retinitis occurred when he was 48. He is now 58, in fair health, and his visual condition, though imperfect, has not prevented his promotion to the post of manager.

Case 18.—I extracted a horny yellowish cataract from this lady's left eye when she was 61 years old, having watched it for 4 years before, during all of which time her urine contained sugar, but the lenticular opacity prevented any useful examination of the fundus of either eye. The operation was quite successful, and she retained useful vision till she died 3 or 4 years afterwards; but I found white patches in the retina within a few weeks of the extraction, and felt sure from the appearance that they were not then new.

Case 33.—This gentleman's retina became affected when he was 59; he is now 66, and still passes a certain amount of sugar, but his sight is reported to have deteriorated little, if at all, since I saw him.

Since many of the subjects of diabetes also pass more or less albumin, and doubt has sometimes been expressed as to whether the retinitis of the diabetic was not in reality caused by coincident renal disease, it is worth mentioning that in 24 fatal cases where I have obtained a definite statement of the immediate cause of death, diabetic coma figures in 11, gangrene in 3, sudden heart failure in several, and acute uncontrollable diarrhœa in 1. In 3 others there is some doubt whether the final comatose condition was uræmic or diabetic. Several other cases died from various pulmonary and cardiac complications. Assuming, as we may safely, that a proportion of direct deaths from diabetic coma also occurred amongst the residue of cases whose record is incomplete, there appears to be no ground for doubting that one-half to three-quarters of the subjects of glycosuria, in whom retinal complications occur, die directly from their diabetes and not from any accompanying renal disease, and the presumption in these is that

the ocular mischief is caused by the principal malady. There is also, as has been already stated,* direct evidence that diabetes alone can cause retinitis in cases where the urine is from beginning to end free from albumin.

* Author, *loc. cit.*

PRIMARY CHANCRE OF THE CONJUNCTIVA AND INTERSTITIAL KERATITIS.

By E. Treacher Collins.

The following case first came under my care at the Moorfields Hospital on October 27th, 1898.

John Y., æt. 24, complained of a sore on the left lower eyelid, which on examination was found to be indurated, having the characteristic appearance of a hard chancre. It was situated near the inner canthus, at the margin of the lid, more to the inner than the outer surface. The pre-auricular gland on the left side was enlarged.

Iodoform ointment was prescribed for application to the sore, and pills containing 2 grains of hyd. c. cret. and 3 grains of pulv. ipecac. a. to be taken internally three times a day.

On November 12th he was found to have a roseola rash on the skin, which he stated had made its appearance a week previously. He also had an ulcerated sore throat. He was told to take the pills four times a day, and continued with them for 2 months, during which time the rash on the skin disappeared. He then ceased attending.

On June 18th, 1900, he again presented himself, stating that for 2 months his left eye had been inflamed.

There was ciliary injection and an irregular mottled haze of the substance of the cornea, with four areas of vascularity ("salmon-coloured patches") at its margin.

The opacity and vascularity at first extended, but subsequently cleared up.

Primary chancre of the conjunctiva is of rare occurrence. Interstitial keratitis in acquired syphilis is also comparatively rare. I am, however, besides the above case, able to refer to 5 others, all recorded within recent years, in which the two were associated.

In all these cases the keratitis was confined to the eye on the side on which the primary lesion was situated.

Lang recorded in the Trans. Ophth. Soc., vol. xi, 1891, and vol. xii, 1892, the case of a man, æt. 42, who had a chancre of the ocular conjunctiva near the caruncle on the right side.

It was followed by secondary symptoms which disappeared under treatment. A year later the right cornea became affected with interstitial keratitis.

Valude recorded in Annales d'Oculistique, January, 1897, the case of a man, æt. 30, who had an indurated chancre at the inner angle of the left eye, followed by roseola and the ordinary train of secondary symptoms. He continued treatment for 2 years; 4 years after the primary lesion interstitial keratitis commenced in the left eye. The affection lasted 1 year, and the right eye did not become involved.

Lawford recorded in the Trans. Ophth. Soc., vol. xx, 1900, the case of a man who had a chancre on the conjunctival surface of the right lower lid. He was treated with mercury.

A sore throat followed, but no rash.

Five months after the first appearance of the primary sore, interstitial keratitis commenced in the right eye. Eight years afterwards, the patient reported his right eye as having got quite well. The left eye had never become affected.

Marlow recorded, in the Ophthalmic Record, vol. xiii, No. 3, p. 113, March, 1904, the case of a woman, æt. 54; she had a characteristic chancre in the lower conjunctival retro-tarsal fold of the right eye. The pre-auricular and sub-maxillary glands were enlarged. She was prescribed for in the usual way, but not seen again until 10 years later, then in the right eye there was typical interstitial keratitis. The left eye was unaffected.

The association of these two rare affections in the above group of five cases would seem to imply more than a chance coincidence.

It would suggest that the proximity of the primary lesion in syphilis to the eye pre-disposes it to become subsequently the seat of an interstitial keratitis.

The fact that, in each case, the keratitis occurred in the eye on the side on which the chancre was situated, and, so far as the history of the cases go, on that side only, is further in keeping with this suggestion.

In connection with this subject, I have another case which is worthy of record, but which differs from the others in that the primary lesion was on the lip instead of the lid.

Lizzie T., æt. 25, attended at the Royal London Ophthalmic Hospital on July 2nd, 1900, complaining of inflammation in her left eye, which had commenced a fortnight previously.

On examination of the eye she was found to have well-marked interstitial keratitis, some ciliary injection, and typical greyish, mottled, infiltration of the cornea.

Her right eye was unaffected.

Her teeth were regular and not notched. There was nothing in her physionomy suggestive of inherited syphilis, with the exception of one slight scar at one angle of her mouth.

She was one of a family of seven, all living, and none of whom had suffered from any eye affection.

She stated that 3 years ago she had had a sore on the upper lip, which was a long time in healing. Afterwards she had a bad sore throat, loss of hair, and a few spots on the skin. While her lip was bad, the glands in front of her ears were swollen.

She was treated for the lip at the Richmond Hospital. On inquiry, the house surgeon of that institution informed me that a patient of her name and occupation was entered as having attended in 1897 with a chancre of the lip.

Six months previous to coming to me, she had, she said, a swelling on the front of the skin of her right leg, which got well with treatment.

She only attended at the hospital on the one occasion, and I do not know the subsequent history of her case.

In these six cases of interstitial keratitis, coming on, undoubtedly, in acquired syphilis, it is interesting to note

the remarkable variation in the time which elapsed between the occurrence of the primary lesion and the onset of the ocular trouble. Thus, in one case it was only 5 months, and in another as much as 10 years.

For sake of comparison, the interval in each case may be given as follows:—

Lang's case, interval 1 year.
Valude's case, interval 4 years.
Lawford's case, interval 5 months.
Marlow's case, interval 10 years.
Collins's (1) case, interval $1\frac{7}{12}$ years.
Collins's (11) case, interval 3 years.

THE INNERVATION OF THE PUPIL.

By J. Herbert Parsons, Curator.

The iris consists of a highly vascular membrane, the blood vessels of which are arranged radially. It also contains two muscles, composed of unstriped fibres—the sphincter and the dilatator. Of these, the former is a compact ring of muscle, situated near the pupillary margin; the latter is a thin layer of muscle, situated near the posterior surface, the constituent fibres being arranged radially. Each muscle has a separate and independent motor nerve supply.

The sphincter is innervated by the third cranial nerve, the pupil-constrictor fibres originating in the third nucleus in the floor of the aqueduct of Sylvius, passing out of the mesencephalon in the third nerve, and running in the main trunk of the nerve as far as the orbit. The fibres here pass into the branch which supplies the inferior oblique, leaving it by the short root of the ciliary ganglion. From the ciliary ganglion, they pass by the short ciliary nerves to the eye, piercing the sclerotic around the optic nerve, and forwards in the choroid and ciliary body to the iris.

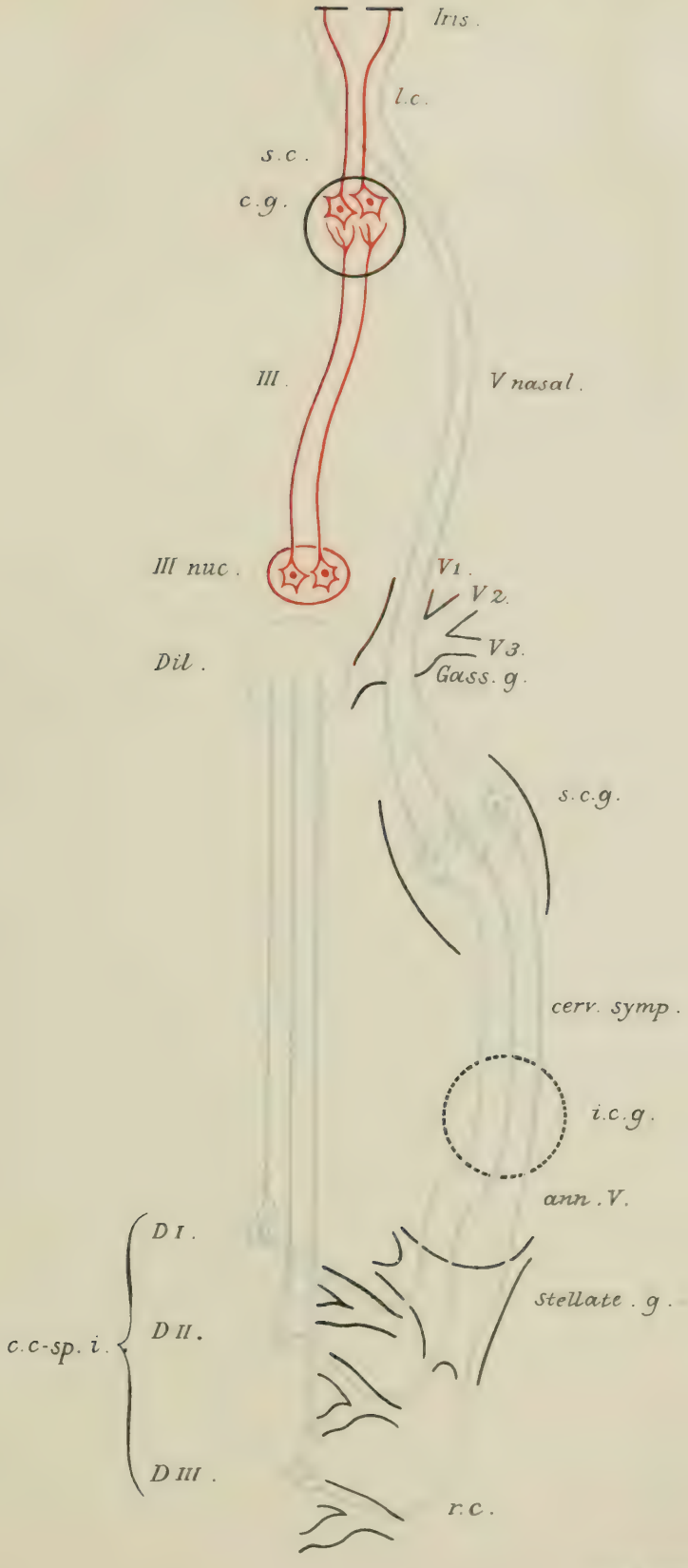
The dilatator pupillæ is supplied by the cervical sympathetic nerve. The dilatator tract probably commences in the neighbourhood of the third nucleus in the mesencephalon, passing through the medulla oblongata, where its exact path is still unknown, into the lateral columns of the cord. The fibres leave the cord by the ventral roots of the first three thoracic nerves (cat, dog, ape), enter the rami communicantes, and run to the first thoracic or stellate ganglion. From here they mostly pass into the anterior limb of the annulus of

PLATE I.

The Efferent Pupillo-constrictor (red) and Pupillo-dilator (blue) Paths.

III. nuc., nucleus of third nerve; *III.* third nerve; *c.g.*, ciliary ganglion *s.c.*, short ciliary nerves.

Dil., hypothetical dilator centre in medulla; *c.c.sp.i.*, centrum ciliospinale inferius; D I, D II, D III, first, second, and third dorsal nerves; *r.c.*, ramus communicans; *stellate g.*, stellate ganglion; *ann. V.*, annulus of Vieussens; *i.c.g.*, inferior cervical ganglion; *cerv. symp.*, cervical sympathetic; *s.c.g.* superior cervical ganglion; *Gass. g.*, Gasserian ganglion; V1, V2, V3, first second, and third divisions of the fifth nerve; *V nasal* nasal branch of the ophthalmic (first) division of the fifth nerve; *l.c.*, long ciliary nerves.



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Vieussens, though some run in the posterior limb. They pass up the neck in the cervical sympathetic to the superior cervical ganglion. From here the dilator tract enters the skull by the cervico-Gasserian strand, running independently of the carotid plexus. It joins the Gasserian ganglion, and passes thence into the first or ophthalmic division of the fifth nerve, following the nasal branch, which it leaves finally to enter the long ciliary nerves, thus avoiding the ciliary ganglion. The long ciliary nerves enter the eye on each side of the optic nerve, and running forwards between the choroid and the sclerotic, pass through the ciliary body to be distributed to the iris. (See Plate I.)

These bald statements are the conclusions arrived at as the result of a vast amount of research during the latter part of last century. In many cases the results have been contradictory, or apparently so, but recent work tends to establish the given statements as incontrovertible facts. There are still, however, many unsolved problems, and these are intimately bound up with the apparently contradictory results of the early experiments. No one attacking the subject afresh can afford to ignore these investigations. It will be well, therefore, to give a brief *résumé* of the evidence upon which the principal statements are founded.

THE MECHANISM OF CONSTRICTION AND DILATATION OF THE PUPIL.—Given constrictor and dilator muscles, each with its own independent nerve supply, together with radially disposed blood vessels, it is clear that constriction of the iris may be due to any of three causes:—(1) contraction of the constrictor muscle; (2) relaxation of the dilator muscle; (3) dilatation of the blood vessels. Similarly dilatation may be due to:—(1) contraction of the dilator muscle; (2) relaxation of the constrictor muscle; (3) constriction of the blood vessels. There is ample evidence to support the view that each of these methods is actually brought into use, and that the three causes are effectual in diminishing degree in the order named.

The Dilatator Pupillæ.—Histological evidence alone has

not succeeded in demonstrating beyond cavil the existence of a dilator muscle in the iris, but taken in conjunction with the physiological evidence it must now be considered proved. The histological difficulties are to be found in (1) the proof of the presence of radial muscle fibres, other than those in the walls of the vessels; and in (2) the interpretation of the nature of the cells forming the posterior layers of the iris.

Maunoir first stated the existence of a circular sphincter and a radial dilator. This view was supported by Valentin (1837), Krohn (1837), Bruch, Brücke, Kölliker, Henle, Luschka, Merkel, v. Hüttenbrenner, Faber, Dogiel, Hulke, Iwanoff, Jeropheeff, and others. It was controverted on the anatomical side by Arnold, Hall, Hampeln, v. Michel, Schwalbe, Koganei, Fuchs, Eversbusch, Retzius, and others. The present state of the question is that the anterior layer of retinal pigment epithelium acts as a dilator muscle (Juler, L. Müller, Gabriélidès, Grunert). On bleaching, the cells of this layer resemble in all respects unstriped muscle fibres. They stain in the same manner, and may be well demonstrated, for example, with Mallory's phosphotungstic acid hæmatoxylin after hardening in Zenker's fluid (Verhoeff). Further, Szili has brought forward evidence to show that the sphincter pupillæ is also derived from the retinal epiblast. These muscles would, therefore, resemble the arectores pilorum of the skin in being formed from epiblast.

The physiological evidence in favour of a distinct dilator contractile tissue in the iris is stronger than the histological, the researches of Langley and Anderson being quite conclusive. Historically it is inextricably mixed up with the vaso-motor theory, so the two are best considered together.

In 1840, Crimelli showed that injection of coloured oil into young eyes (children) caused constriction of the pupil; and Rouget (1866) proved the same fact by injecting fluid into the ophthalmic artery. The early literature will be found in the papers of Zeglinski and Heese.

Grünhagen, in a series of papers from 1864 to 1893,

warmly supported the vaso-motor theory, whereby a diminished quantity of blood in the vessels leads to shrinkage of the iris. It is clear also that constriction of the arteries, accompanied by contraction of the longitudinal muscle fibres in their walls, may lead to dilatation of the iris by dragging the sphincter outwards (Langley and Anderson). Budge and Waller (1851) and Budge (1855) proved that dilatation through the sympathetic can occur in the absence of variations of blood supply, *e.g.*, after death. Waller (1856) showed that making the iris of a white rat bloodless by pressing upon the eye had no effect upon the pupil. Brown-Séquard (1859) found barely appreciable constriction of the pupil on injecting blood into the ophthalmic artery, though the effect is greater a day or two after death (Mosso, 1874). François-Franck (1880) obtained dilatation through the sympathetic after bleeding the animal to death.

Claude Bernard (1852), and Waller (1853) demonstrated vaso-motor nerves to the ears, etc., and Kuyper (1859) to the iris, in the cervical sympathetic. Salkowski (1867) also proved that constriction of the vessels accompanied dilatation of the pupil, Donders noting the same fact in albino rabbits, and Becker in human albinoes. Sinitzin showed that excision of the superior cervical ganglion was followed by dilatation of the vessels. Arlt. Jr. (1869) and François-Franck (1880) proved that dilatation of the iris and constriction of the vessels of the ear do not occur synchronously. Langley and Anderson (1892) proved the same fact for the iris vessels, showing at the same time that no deductions can be made as to time relations from the vessels of the ear.

There is evidence that the vaso-motor and pupillo-dilator fibres run independent paths. Bernard (1862) found in the dog that section of the first and second thoracic nerves caused dilatation of the pupil, but no vascular change in the skin of the head, whereas section of the thoracic sympathetic between the second and third ribs caused the reverse effects. Langley and Anderson (1892) showed that dilatation of the

pupils and distinct constriction of the vessels of the iris were caused by the first three thoracic nerves, and by these only; but the readiness and extent of the pupillary dilatation was not proportional with the several nerves, to the readiness and extent of the arterial constriction. Schiff (1872) showed that the two sets of fibres could occasionally be isolated as separate bundles in the cervical sympathetic, and one or other effect obtained alone. Budge and Waller (1851) found that the pupillo-dilator fibres, after leaving the superior cervical ganglion, accompanied the internal carotid artery in its canal, running to the Gasserian ganglion; whilst François-Franck (1880) showed that the superior cervical ganglion gives off two strands to the carotid canal, and the external causes dilatation of the pupil, but no increase in pressure in the peripheral end of the carotid, the other strand causing the reverse effects. François-Franck also found separation of the two tracts in the annulus of Vieussens, but these experiments are inconclusive (Langley and Anderson). Some of the short ciliary nerves cause constriction, others dilatation of the pupil, according to François-Franck, whilst neither cause variation of the retinal vessels or change in intra-ocular pressure. These experiments are also inconclusive. Jegorow (1886) found that after section of the long ciliary nerves, stimulation of the central end of the vago-sympathetic causes strong contraction of the retinal vessels, but no pupillo-dilatation, whilst stimulation of the peripheral end of a long ciliary nerve causes the reverse effect.

Waller (1856) and Vulpian (1873) noticed in the white rat that no constriction of the iridic vessels accompanies dilatation of the pupil by atropin. Langley and Dickinson (1890) showed that intravenous injection of brucin may eliminate pupillo-dilatation from the sympathetic, the vaso-constriction of the vessels of the ear still remaining, and Langley and Anderson (1892), by the same method, were able to obtain complete constriction of the vessels of the iris without any change in the size of the pupil.

Even if the relative unimportance of the vaso-motor changes be conceded, the dilatation of the pupil may be due to inhibition of the sphincter pupillæ. This possibility was announced by Grünhagen and Samkowy (1875), without further investigation, except that they showed that the tone of the sphincter can be diminished by direct stimulation, the muscle becoming elongated. François-Franck (1880) expressed the same view with some reserve, whilst Gaskell (1886), influenced largely by dubious analogies, definitely advanced the inhibitory theory. Kölliker (1855) had already obtained dilatation after removal of the sphincter, but the conditions of the experiment prevent its being accepted as positive evidence. The inhibition of antagonists on stimulation of muscles is definitely proved in many cases, and inhibition of the sphincter tone is also proved, but whether the cervical sympathetic has this property must still be considered *sub judice*, though with distinct bias to the negative. In any case it would afford no disproof of the existence of a dilator muscle.

The possibility of pupillo-dilatation as the result of relaxation of the ciliary muscle was advanced and controverted by Langley and Anderson (1892).

Most important are the experiments which definitely prove the existence of a contractile dilator mechanism. Weber first showed that stimulation of the sclerotic near the limbus caused dilatation of the pupil, whilst stimulation of the cornea was followed by constriction of the pupil. Bernstein and Dogiel (1865–67) found that the result might be varied by other arrangements of the electrodes (see Langley and Anderson (1892)); their experiments were confirmed by Engelhardt (1869).

Local dilatation can be obtained by other means. Hensen and Völkers (1868) found it on stimulating a single ciliary nerve, but this may be followed by general dilatation or general constriction (François-Franck). Jegorow (1886) obtained local dilatation in the dog from stimulation of a single long ciliary nerve; on section of all but one ciliary

nerve, subsequent excitation of the cervical sympathetic or of a sensory nerve causes well-marked local dilatation.

The effects of stimulation of the sclerotic near the cornea have been exhaustively investigated by Langley and Anderson (1892). They obtained: (1) Movement of the iris on the side opposite to local dilatation, which was of such a nature that it could not be explained by inhibition of the sphincter in the presence of radial elastic fibres; (2) local dilatation of the pupil with simultaneous local contraction of the sphincter: (3) contraction of a radial strip of the iris. They also proved the absence of any great elasticity in the iris, such as might account for some of the results on the theory of sphincter inhibition.

The Efferent Pupillo-Constrictor Path. *The Third Nerve.*—Romberg (1851), in his text-book on "Nervous Diseases," refers to dilatation of the pupil as a symptom of paralysis of the third nerve. Budge (1851) states that constriction of the pupil follows stimulation of the third nerve in recently killed animals and man; this observation was confirmed by v. Trautvetter (1866). Schiff (1868) thought that the iris fibres were on the inner side of the trunk of the nerve, since section of the inner fibres caused paralysis of the iris movements without abrogating the movements of the globe. Hensen and Völkers (1868) found pupil constriction from stimulation of the ciliary ganglion and the short ciliary nerves; excitation of single short ciliary nerves caused local constriction, whilst section caused local dilatation. Adamük (1870) confirmed the importance of the ciliary ganglion: he further stimulated the origin of the third nerve in the floor of the aqueduct of Sylvius, and adduced evidence to the effect that the pupillary fibres passed backwards from the nucleus on their way to the trunk of the nerve. Hensen and Völkers (1878) proved that the fibres pass forwards rather than backwards, Adamuk's results being due probably to stimulation of afferent fibres running forwards in the medulla to join the centre.

This course for the pupillo-constrictor fibres has been confirmed by all subsequent observers, the only discovery of importance being that there is a cell station in the ciliary ganglion. This was proved by Langley and Anderson (1892), both by the nicotin method and by the degeneration method. If the third nerve is cut within the skull, many degenerated fibres are found running to the ganglion, but none peripherally of it (Apolant, 1896). The preganglionic fibres running from the third nerve to the ciliary ganglion are mostly small medullated fibres. The postganglionic fibres running in the short ciliary nerves are three or four times as numerous as the preganglionic ones, and also consist chiefly of small medullated fibres. These facts were stated by Bidder and Volkmann (1842). These autonomic (Langley) postganglionic fibres differ, therefore, from the rule which applies, though with many exceptions, to the postganglionic fibres of the sympathetic system in being medullated.

Further proof of the origin of the postganglionic pupillo-constrictor fibres in the cells of the ciliary ganglion is afforded by the Nissl method. This method is extremely delicate, but demands the greatest care in the interpretation of the results. In this case it gives valuable confirmatory evidence; in others the conclusions deduced from it must be accepted with reserve. There is even considerable divergence of opinion in the results of experiments upon the ciliary ganglion. Thus Bach (1899) found that nearly all the cells were degenerated after excision of the iris and ciliary body; none when the cornea was removed. Marina (1899–1901) found degeneration from destruction of the cornea, but much more after iridectomy. Bumm (1902) counted the cells and found the normal average to be 6432. After cutting the ciliary nerves, 3854 remained unaffected; after excising the superior cervical ganglion, the cells were reduced to 2587. The latter result may be due to the removal of afferent impulses (*cf.* Warrington).

Paradoxical Pupillo-Constriction. — Under ordinary

conditions the pupillo-constrictor centre emits tonic impulses, so that when these are cut off by section of the constrictor path in any position the pupil becomes slightly larger than normal. It has occasionally been observed that the pupil is smaller than normal; this is called paradoxical pupillo-constriction. It has been less frequently seen than paradoxical pupillo-dilatation, to which reference will be made later.

Paradoxical pupillo-constriction has been investigated by Anderson (1902), only an abstract of his results having been as yet published. He found that after excision of the left ciliary ganglion and section of the right third nerve proximally of the ganglion in a kitten, the two pupils were equally dilated until regeneration occurred on the right side 8 days later. In a cat the right pupil continued to be widely dilated 38 days after division of the right short ciliary nerves. Under certain circumstances, however, the pupil on the side of the excision was smaller, *e.g.*, in the cat the right pupil was smaller in dim light than the left after local application of eserin to both eyes in equal quantity; and 18 days later the right pupil was smaller after the death of the cat.

In another cat the left pupil immediately after excision of the left ciliary ganglion was very widely dilated, but next day the left pupil had become slightly smaller, and was smaller than the right in dim light if the cat became restless under observation. On the same day after administration of ether and section of both cervical sympathetic nerves the left pupil became a slit, though the right was almost maximally dilated, and for 48 hours after death the left pupil remained much smaller than the right.

In other observations made 2 and 318 days after denervation of the sphincter on one side, the pupil on the side of the lesion was smaller after the death of the animal, though previously it had been the larger since the denervation.

Anderson concludes that the paradoxical pupillo-

constriction is due to increased excitability of the denervated sphincter, the exciting stimuli in the observations mentioned being alterations in the blood supply, eserin, and probably ether (see, however, the observations on paradoxical pupillo-dilatation).

THE EFFERENT PUPILLO-DILATOR PATH.—Investigations on the pupillo-dilator path have been attended with more ambiguous results than those on the constrictor path.

The Cervical Sympathetic Nerve.—Parfour du Petit (1727) first showed that section of the cervical sympathetic was followed by constriction of the pupil upon the same side, as well as by other symptoms which do not concern us here. The observation was confirmed by Molinelli (1755), Arnold, Stilling and others. Valentin pointed out that section caused a short and transitory dilatation of the pupil, followed by constriction which remained permanent. Serafino Biffi (1846) repeated Petit's experiments and confirmed them, and further supplemented them by showing that stimulation of the sympathetic causes dilatation. Reid (1848) isolated the sympathetic from the vagus fibres in the cat, and showed that only the sympathetic caused dilatation of the pupil on stimulating the peripheral end.

Budge (1851–55) first seriously attacked the problem of the innervation of the pupil, and it is only within the last few years that anything of importance has been added to his results, though they have been corrected in details. He found that if the spinal cord between the sixth cervical and the fourth thoracic vertebræ is isolated by transverse section above and below, then stimulation of this area causes dilatation of both pupils, which is abrogated on one side if the corresponding sympathetic is cut. Stimulation of the cord above or below this region caused no effect. Hence Budge concluded that there was a centre for the dilatation of the pupil here; he called it the *centrum cilio-spinale inferius.* He also traced the dilator fibres from this centre to the cervical sympathetic, showing that they leave the cord by the anterior roots of the seventh and eighth cervical

and first and second thoracic nerves; Budge also described a *centrum cilio-spinale superius*, which he thought was in the region of the nucleus of the hypoglossal nerve. He thought that the superior cervical ganglion received pupillo-dilator fibres directly from this centre as well as from the inferior one through the sympathetic. The experiments upon which the idea was founded are open to another interpretation, and afford no evidence of a superior centre. Schiff (1855) confirmed Budge's results, but opposed his idea that the centrum cilio-spinale inferius was an automatic and independent centre. He gave good evidence to show that it was under the control of impulses descending from above, so that hemisection of the cord above the fourth cervical vertebræ caused constriction of the pupil on the same side, and the other effects of cutting the sympathetic. He therefore considered that the superior centre alone was automatic.

The complete demonstration of the dilator path was intimately bound up with the discovery and investigation of the sensory pupillary reflex, which must, therefore, be referred to in this connection. Chauveau (1861) discovered that dilatation of the pupil followed excitation of the posterior columns of the cord; this only occurred with the intact cord in his experiments. (It had long been known that pupil dilatation often occurred in trigeminal neuralgia (Notta, 1854)). Claude Bernard (1862) first showed that excitation of the central end of any sensory nerve caused dilatation of the pupil; he found that the effect was abolished by section of the anterior roots, which are known to carry the pupillo-dilator fibres.

Balogh (1861) noticed dilatation during asphyxia, even if the superior cervical ganglion had been removed. Stimulation of the trunk of the fifth nerve, or of the Gasserian ganglion, or of the ophthalmic division of the fifth, caused dilatation. If the trunk of the fifth nerve was cut, stimulation of the medulla caused no change in the pupil. He therefore arrived at the deduction that the fifth, nucleus is the upper centre for the dilator fibres, and that the dilator

fibres all pass through the Gasserian ganglion and thence into the ophthalmic division of the fifth.

Oehl (1862) obtained dilatation of the pupil from the first division of the fifth after excision of the superior cervical ganglion; there were no dilator fibres in the trunk of the fifth nerve. Hence he concluded that the dilators arise in the Gasserian ganglion—an erroneous deduction. Guttman (1864) supported this view; he opposed the medullary centre and found slight pupillo-constriction after dividing the fifth just proximal to the Gasserian ganglion.

Salkowski (1867) confirmed Budge's experiments and supported the view of the medullary centre, which he found to be the reflex centre for the sensory stimuli. He asseverated the existence of a single pupillo-dilator path from the medulla through the centrum cilio-spinale inferius to the cervical sympathetic.

Nawalichin (1869) confirmed Balogh's results and fell into several errors. He found that the sensory reflex was eliminated by section of the cord above the spinal centre of Budge, and also that the sympathetic is not the only dilator tract. The latter view was founded upon two chief observations: (1) if the cord is cut at the level of the third cervical vertebra, stimulation of the upper cut end causes dilatation; (2) if the cord is cut below the medulla, asphyxia still causes pupillo-dilatation. Both of these observations are correct, but they are open to other interpretation. Vulpian (1874) also thought that the trunk of the fifth nerve contained dilator fibres, both from his experiments in which it was cut, and also because the sensory reflex from the sciatic nerve persisted after extirpation of the superior cervical and stellate ganglia.

Hurwitz (1878) repeated Vulpian's experiments, and performed two new ones which are of some importance. If the superior cervical ganglion was removed, then after at least 120 hours' interval it is found that direct stimulation of the iris of the atropinised eye of a curarised animal causes not the slightest trace of dilatation. If the sympathetic is cut

a few days before stimulation of a sensory nerve, pupillo-dilatation is not abolished, but is slower in onset and more prolonged.

Schiff and Foa (1874) devoted special attention to the sensory reflex, and found that the pupil may be regarded as an æsthesiometer. They confirmed Chauveau's result that the afferent path runs in the posterior columns of the cord, adding also the grey matter; they obtained no sensory reflex after section above or below the medulla.

François-Franck (1878–80) made an exhaustive investigation of the whole subject. The results which concern us here are as follow. From the fact that section of the trunk of the fifth nerve is followed by constriction of the pupil, he concluded that that nerve contains dilator fibres. He also found dilator fibres in the vertebral nerve. He showed that the dilators pass by the rami communicantes of the fourth cervical to the sixth or seventh thoracic in cuts to the thoracic sympathetic. Thence they pass into the stellate ganglion, and from there, by the anterior limb of the annulus of Vieussens, to the cervical sympathetic. He found no pupillo-dilators in the posterior limb of the annulus, but this is untrue (Langley and Anderson). The sympathetic receives no other dilator fibres in the neck. All the ciliary nerves are pupillo-constrictors with the exception of two or three. The short ciliaries cause rapid constriction, whilst the long ciliaries cause slow dilatation. Extirpation of the stellate, or of the superior cervical ganglion, causes greater dilatation of the pupil than simple section of the sympathetic nerve; hence he concludes that these ganglia exert a tonic influence over the irido-dilator mechanism. Guillebeau and Luchsinger (1880) ascribed the dilatation from the vertebral nerve to sensory fibres contained in it.

Luchsinger (1880) supported the view that the inferior cilio-spinal centre is automatic. He obtained the sensory reflex after section of the cord, if the excitability is increased by picrotoxin or strychnin. Tuwim (1881) failed to obtain dilatation from sensory stimuli after cutting the cord. He

confirmed the discovery of François-Franck that the superior cervical ganglion exerts a tonic influence; he found the pupil smaller on the side in which the ganglion was extirpated than on the side in which the sympathetic was cut. Guillebeau and Luchsinger (1882) obtained the sensory reflex in young cats after section of the cord without artificially increasing the excitability of the cord, and this result was also found in cats by Ott (1882).

Sheglinski (1885) showed that the pupillo-dilators in birds run in the first division of the fifth. They do not run in the cervical sympathetic. This statement was controverted by Grünhagen, but has been substantiated by Langley (1903). It was also confirmed by Jegorow (1886), who found vaso-motor fibres in the sympathetic, but no pupillo-dilators. This observer also confirmed the course of the dilators in mammals in the ophthalmic division of the fifth, and in the long ciliary nerves.

Bellarminow (1886) first used the photographic method for recording the pupillary movements. He distinguishes between (1) direct (sympathetic) dilation and (2) reflex dilation. The latter occurs whether the sympathetic is intact or not. He found that the pupil varies independently of the blood pressure or the intraocular pressure.

Katharina Schipilow (1886) traced the dilators in the frog. She found no difference between cutting the sympathetic and excising the sympathetic ganglia.

Nawrocki and Przybylski (1891) found that in cats the dilators leave the cord by the ventral roots of the eighth cervical and first and second thoracic nerves. The fibres do not pass through the ciliary ganglion, but enter the long ciliary nerves. These authors also admit a cranial dilator path, though they deny the presence of dilators in the vertebral nerve. There is a centre in the brain, but there are no sufficient grounds for supposing that there is an inferior cilio-spinal centre.

Braunstein (1894) re-investigated the whole subject in an extremely careful research, using Bellarminow's photo-

graphic method. He found the dilator fibres in the rami communicantes of the seventh and eighth cervical and first and second thoracic nerves of the cat. He found no dilators in the posterior limb of the annulus of Vieussens. Above the superior cervical ganglion the dilators run in a special branch, separate from the carotid branches, to the Gasserian ganglion. Stimulation of a long ciliary nerve caused partial dilatation (as opposed to general dilatation found by François-Franck and Bellarminow).

The pupillo-dilator fibres in the cervical sympathetic end around the cells in the superior cervical ganglion. This has been proved by the degeneration method by Waller and Budge (1851–53), and by the nicotin method by Langley and Dickinson (1899–1900).

Langley (1892, sqq.) found the dilator fibres in the first three thoracic nerves. In the cat and dog the third has much less effect than the other two; in the rabbit, and apparently in the ape, the third may have a greater effect than the first, but never so great an effect as the second. It has already been mentioned that Langley and Anderson (1892) found dilator fibres in the posterior limb of the annulus of Vieussens, as well as in the anterior limb, though they were not so numerous.

The preganglionic fibres of the cervical sympathetic, including, therefore, the pupillo-dilator fibres, consist of fine medullated fibres. The postganglionic fibres in the branches from the superior cervical ganglion consist for the most part of non-medullated fibres. Degeneration of these fibres has been specially investigated by Tuckett (1896).

By the Nissl method, according to Marina, some of the cells of the superior cervical ganglion degenerate when the ciliary nerves are cut.

The Fifth Nerve.—We have already seen that several observers considered that there were pupillo-dilator fibres in the fifth nerve. Magendie (1824) first proved that section of the fifth within the skull in the rabbit caused constriction of the pupil. This was denied by Longet

(1842). Valentin and Claude Bernard showed that the effect was transitory, whilst the effect of section of the ophthalmic division of the fifth was lasting. Balogh, Nawalichin, Vulpian, and François-Franck all confirmed the presence of dilators in the trunk of the fifth. Schiff (1867) thought they were sympathetic fibres from the cavum tympani. Rembold (1880) agreed with Schiff that the tone of the dilator was kept up by afferent sensory stimuli, explaining thereby the miosis which follows section of the fifth. In order to explain the constriction caused, according to several authors, by excitation of the trunk of the fifth, he considered it probable that there were actually pupillo-constrictor fibres in the fifth nerve. Eckhard (1892) also thinks that there are constrictors in the fifth.

It is unnecessary to enumerate all the authors who consider that there are dilators or constrictors in the trigeminal. Braunstein and Hurwitz may be held to have proved their absence. Further, Langley could not obtain local dilatation of the pupil from stimulation of the sclerotic after excision of the superior cervical ganglion some time before, and Anderson failed to obtain it even on stimulating the iris under the same conditions. Other observers, amongst them myself, have failed to obtain any movement of the pupil after section of the third nerve and the cervical sympathetic. It may, therefore, be considered definitely proved that all the dilator fibres run in the cervical sympathetic.

Paradoxical Pupillo-Dilatation.—Paradoxical pupillo-dilatation is the antithesis of paradoxical pupillo-constriction. "Section of the cervical sympathetic causes constriction of the pupil, and simultaneous removal of the superior cervical ganglion on the other side causes slightly greater constriction, as first shown by Budge, but in certain circumstances the pupil on the side without the ganglion becomes larger than the pupil on the side with the nerve alone cut. This greater dilatation on the more paralysed side has been called parodoxical pupil-dilatation by Langendorff. Moreover, if only a superior cervical ganglion be excised, the pupil on the

paralysed side may nevertheless become larger in certain circumstances than the normal pupil. This is also spoken of as paradoxical dilatation." (Anderson.)

Budge (1855) first called attention to the occurrence of paradoxical pupillo-dilatation. After section of the left sympathetic and of the branches above the right superior cervical ganglion in a young rabbit he found the right pupil smaller than the left $\frac{1}{2}$ hour later, equal after 24 hours, and the right larger than the left after 48 hours. Schiff (1868) observed the effect after section of the sympathetic, and after excision of the ganglion; he connected the phenomenon with oxygenation of the blood after previous asphyxiation. Surminski (1869) and Tuwim (1881) observed it after atropin. Kowalewski (1886) saw it in a kitten after the administration of chloroform. Braunstein (1894) observed it after curare; and Tuckett (1896) incidentally in the course of another research. Langendorff (1900) investigated the subject specially, and noticed the phenomenon after anæsthetics and after death. Lewandowski (1900) also called attention to these paradoxical effects, and showed that they could be produced by dyspnœa. It was also observed incidentally by Langley (1901) and Levinsohn (1902).

The subject has been exhaustively investigated recently by Anderson (1903). He proved that the effect might be observed as soon as 1 day after the lesion, and as long as more than a year. Excitement, dyspnœa, anæsthesia, death, are conditions which evoke the effect. It is produced much more readily by slight dyspnœa in kittens than in cats. The paradoxical effect persists even when the postganglionic branches of the ganglion have been allowed to regenerate. Immediately after removal of the ganglion on one side, and section of the sympathetic on the other, there is always greater paralysis on the side without the ganglion. Later there is frequently greater paralysis on the side with the nerve cut, but if sufficient care is taken to insure a quiet condition of the cat, the signs of greater paralysis are often transferred to the side without the ganglion.

In the quiet condition of the cat the evidence is therefore often against the views (1) that the sphincter is weakened on the side without the ganglion (Budge, Tuwim, Levinsohn), or (2) that there is permanent contracture of the vessels of the iris, or dilatation on this side (Surminski, Langendorff), or (3) that on the side with the ganglion the dilator is inhibited (Kowalewski).

After the local application of eserin to the eyes of a kitten the pupil is smaller on the side from which the superior cervical ganglion has been removed so long as the kitten is quiet, but slight dyspnœa will cause the pupil to become almost maximal though the normal control pupil is very small. A similar result may be obtained when the sphincters are contracting strongly in bright light instead of under the influence of eserin.

This paradoxical pupillo-dilatation must therefore result from an actual increase of tone in the dilator on the side without the ganglion. This increase of tone may be directly demonstrated in the nictitating membrane and lids. The paradoxical effect is therefore due to an increased excitability of the contractile tissues on the side without the ganglion (Lewandowski, Anderson).

The great accentuation of the paradoxical effect seen under anæsthesia does not occur until dyspnœa arises. If only the sympathetic has been cut, the paradoxical effects occur much later, and are much less pronounced.

The paradoxical effects show that the ganglion cannot inhibit the automatic excitability of the contractile tissues with which it is still in connection.

Bright light cannot inhibit the paradoxical dilatation through the third nerve, since the effect will still persist in bright sunlight for more than a minute.

Inhibition of Antagonists.—It is known that in the case of the skeletal muscles contraction of a given group is accompanied by simultaneous active relaxation of the antagonistic group (Sherrington). By analogy, therefore, it is not improbable that constriction of the pupil through the

third nerve should be accompanied by simultaneous active inhibition of the dilator, also carried out through the third nerve by means of inhibitory dilator fibres. And, indeed, Waymouth Reid (1895), from consideration of the electrical phenomena occurring during contraction of the sphincter, concluded that this actually happened. Anderson (1903), however, has brought forward strong arguments against this view. Thus, using bright light as a stimulus to contraction of the sphincter, it is found that the paradoxical dilatation may arise and continue for more than a minute in bright sunlight; and further, under the same conditions, a difference between the two pupils caused by paralysis of one dilator is not diminished, but increased by brighter illumination of the eyes. Neither of these observations is consistent with inhibition of the sphincter through the third nerve.

The iris is not under the control of the will, hence these motor nerves are invariably set in action indirectly, either by reflex stimuli, or by what I shall call *synkinesis, i.e.*, association with other voluntary or involuntary movements.* There are two chief reflexes, and two chief synkineses or associated movements. (1) The Light Reflex; (2) The Accommodation Synkinesis; (3) The Sensory Reflex; (4) The Cerebral Synkinesis.

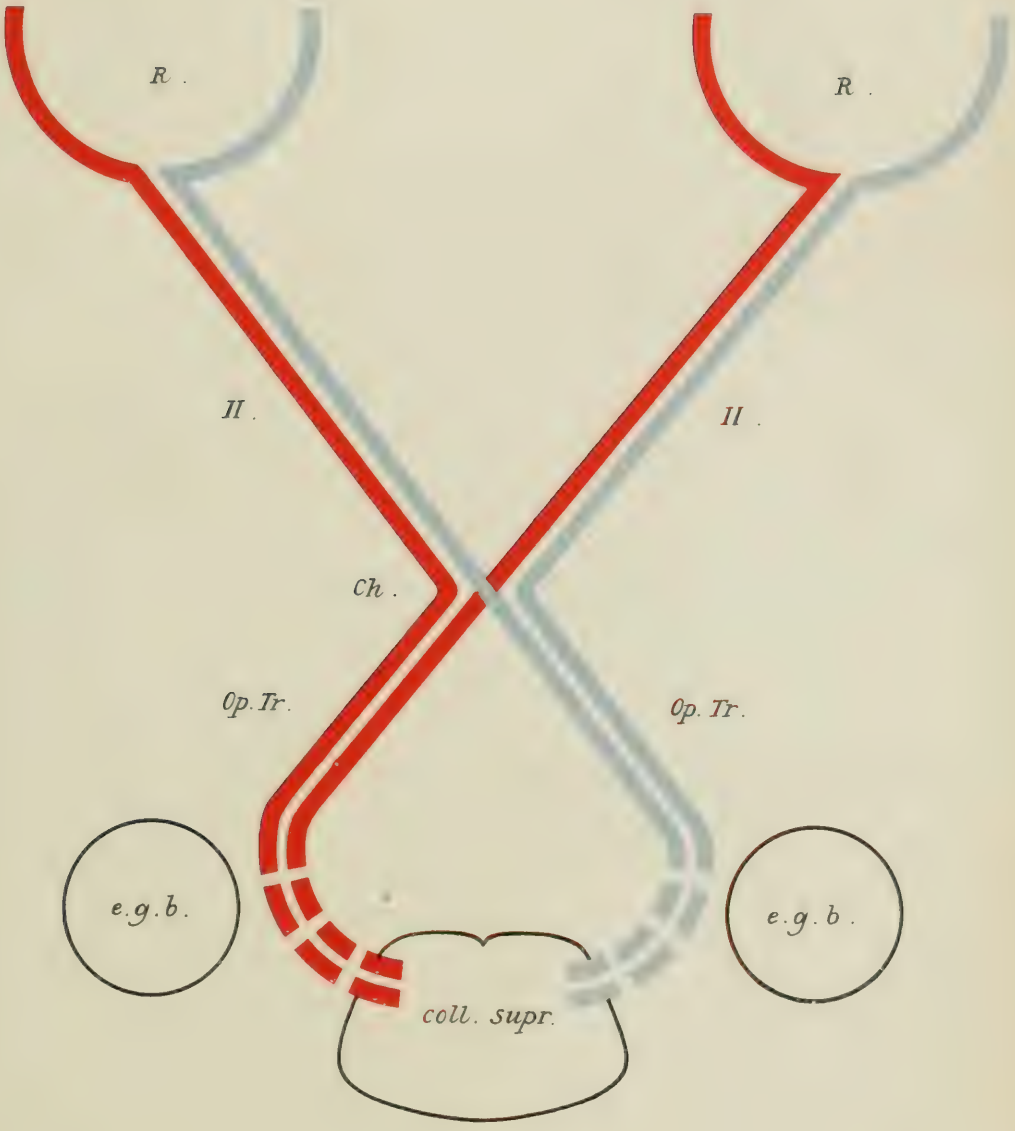
The Light Reflex is carried out entirely through the mechanism of the constrictor centre. Of the afferent paths we know very little for certain. The fibres are contained in the optic nerve, and they arise from all parts of the retina. The optic nerve contains large and small fibres; it is possible that the large fibres are concerned with visual sensations, and that some of the fine ones are afferent pupillo-constrictor fibres. The opposite view has also been advanced. It is certain that the pupillary fibres undergo partial decussation

* The corresponding term for the association of ideas, or an associated idea, would obviously be *synpsychosis*.

PLATE II.

The Afferent Pupillo-constrictor Path.

R., retinæ; *II*, optic nerves; *Ch.*, chiasma; *Op. Tr.*, optic tracts; *e.g.b.*, external geniculate bodies; *coll. supr.*, superior colliculus or anterior quadrigeminal body.



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in the chiasma, and enter the optic tracts. It is also certain that they do not enter the lateral geniculate body, but leave the tract to pass by a path which is as yet conjectural to the third nucleus. The tone of the constrictor centre is kept up by constant afferent impulses along this tract; it is possible that it also possesses inherent tone. The tone is probably continually depressed by less effectual impulses along the fifth and other sensory nerves.

There are two types of light reflex, viz., that through the retina of the same side, or the direct reflex, and that through the retina of the opposite side, or the consensual reflex; *i.e.*, light falling upon the retina causes constriction of the pupil —a direct reflex, but it also causes constriction of the opposite pupil—a consensual reflex.

Lambert (1760) found that the constriction increased with the area of the retina which was stimulated. E. H. Weber (1851) found that it was stronger the nearer the affected part lay to the macula, and was strongest of all when the luminous body was the object of fixation.

Herbert Mayo first obtained constriction of the pupil from experimental stimulation of the optic nerve. Flourens (1824) placed the reflex centre in the corpora quadrigemina, a view concurred with by Longet, Budge, and others. Knoll (1869) showed that the whole anterior colliculus might be destroyed without preventing the light reflex. This was confirmed by v. Bechterew (1884) and others—recently by Ferrier and Turner (1901).

The Afferent Pupillo-Constrictor Path (Plate II).—The fact that, like the afferent visual fibres, the afferent pupillo-constrictor fibres undergo partial decussation in the chiasma is proved by the hemiopic pupil reaction of Wernicke. This observer found that any lesion which destroyed one optic tract caused loss of the light reflex on stimulation of the corresponding halves of both retinæ, whilst stimulation of the opposite halves gave the normal reaction. Attention was called to the fact that the pupillary and visual paths are not identical by the effects of destruction of the superior

colliculi, and this was confirmed by the effects of destruction of the lateral geniculate body. I have in the first lecture given additional evidence that the visual fibres divide, probably more frequently than has hitherto been supposed. It is not improbable that the pupillary reflex is carried out by means of collaterals.

In any case, destruction of the lateral geniculate body does not abolish the light reflex (v. Bechterew, Henschen and others). Hence the pupillary fibres leave the tract before it reaches the geniculate body. Bogroff and Flechsig (1886) describe a tract passing directly into the stratum griseum centrale of the third ventricle. According to an earlier view of v. Bechterew (1883), the fibres do not enter the optic tract, but pass into the grey matter of the third ventricle close behind the chiasma. Such a view is negatived by the Wernicke reaction, and has apparently been abandoned by v. Bechterew (1900); he now thinks they leave the optic tract at the level between the corpus cinereum and the root fibres of the third nerve, *i.e.*, near the entrance of the optic tract into the geniculate body, running thence to the posterior part of the third ventricle, where they make connections with cells which send axones to the third nucleus of the same side.

Darkschewitsch (1886) thinks that the pupillary fibres leave the optic tract near the geniculate body and pass through the thalamus to the ganglion habenulæ. Thence fresh fibres pass through the posterior commissure to his obere Oculomotoriuskern. This, however, has been shown by v. Bechterew and others to have nothing to do with the third nerve. His results have been supported on comparative anatomical grounds by Bellonci, and also by Mendel.

The evidence is in favour of the afferent pupillo-constrictor fibres making new connections before reaching the third nucleus. Bernheimer (1899), however, thinks that they pass direct to the third nucleus, but Bach (1900) was unable to confirm his results. It must be admitted that the question is by no means settled. It seems most likely that

the fibres pass through the superior brachium into the superior colliculus, there making new connections with cells which convey the impulses to the third nucleus of the same and also of the opposite side. This view is held by Barker, and is probable from the histological researches of Held. It would account satisfactorily for all the facts, including both the consensual reaction and the hemiopic pupil reaction. The effects of extirpation of the superior colliculus are not necessarily fatal to this theory. It is most probable that the afferent pupillary fibres end in the lateral part of the colliculus, and this may quite easily have escaped destruction in experiments in which it is so important that the lesion should be strictly localised.

The Pupillo-Constrictor Centre.—I do not intend to attempt in this lecture to unravel the tangle of speculations as to the reflex pupillary centres. The number of these centres which have been described and localised by various writers, each with the utmost assurance, is bewildering in the extreme. To name only a few, we have several constrictor centres, several dilator centres, not to mention various cortical and sub-cortical centres of each kind, and finally Bach has added to the confusion by hypothecating an inhibitory constrictor, and even in his last paper an inhibitory dilator centre. The explanation is to be found in wild theorising upon quite inadequate data, and much of this is due to the use of the unfortunate term "centre." One is inclined to wish that this term might be abolished from neurology, so great is the ambiguity and confusion to which it has given rise. The intercommunications between the cells of the central nervous system are so complex that there are almost innumerable alternative paths whereby any given group of efferent cells may receive excitatory impulses. Our aim should be, first to determine the efferent cells governing any given movement, second to determine as far as is possible which are the afferent tracts which can lead directly or indirectly to those cells, and third to find out *how* each of those afferent tracts leads to the efferent cells. The last

problem is the most difficult, and we shall find that many of the afferent tracts are very devious, and have many cell-stations on their way. Each of these may be dignified with the title "centre," or better, none of them.

There are one or two points, however, which must be mentioned in spite of the obscurity of the subject. We have seen that the third nerve contains all the constrictor fibres for the iris. We have reason to believe that the light reflex is an active constrictor effect and not an inhibitory dilator effect: for, seeing that probably both centres exert a tonic influence, it is obvious that the result might arise from either of these causes. If this reasoning is sound, the only true centre for the light reflex is the part of the nucleus of the third nerve which gives rise to the pupillo-constrictor fibres. Most authors are inclined to agree that this is the Edinger-Westphal nucleus, which consists of small cells occupying the median part of the third nucleus. It may be subdivided into two parts, an anterior paired nucleus and a posterior unpaired nucleus. The former, according to Bernheimer, contains the pupillo-constrictor cells.

This view is not universally adopted, and there are still some—chiefly neuro-pathologists (*e.g.*, Sacki and Schmaus, Schaffer), who adhere to the inhibitory dilator theory, or a modified form of it. Argyll Robertson (1869) must be considered principally responsible for this view, which he held best explained the pupil phenomenon which bears his name. Pathological evidence in favour of it has been collected by Wolff (1899), and it has received some support from the (inconclusive) experiments of Bach, Ruge and others.

Marina (1901–3) thinks that the ciliary ganglion is the centre for the light reflex, and he brings forward some ingenious experiments to prove his point. They cannot, however, be considered conclusive.

Very conclusive evidence in favour of the supreme importance of the third nucleus in the light reflex is afforded by the fact that variations in illumination have no effect on the pupil after section of the third nerve (Braunstein and others).

Anderson (1903) points out the necessity for care in eliminating all tactile and other sensory reflexes in these experiments. They prove that the light reflex is entirely through the pupillo-constrictor mechanism, and that inhibition of the dilator tone plays no part. This is additional evidence that the sphincter and dilator do not follow the law of contraction and relaxation of antagonists (see p. 46).

The Accommodation Synkinesis is a constrictor effect commonly associated with accommodation. It is more nearly related, however, to the convergence which normally synchronises with accommodation, since it is possible to accommodate without inducing constriction of the pupil, whereas this invariably occurs during convergence. Very little is known about this phenomenon; even the views stated are open to doubt, but there can be no doubt that it is not a true reflex, but a case of associated movement. The same remark applies to the well-known lid-closing phenomenon.

The accommodation synkinesis has been known since Scheiner (1619). The efferent fibres for accommodation were investigated by v. Trautvetter (1866), Hensen and Völkers (1868, 1878), Kaiser (1868), Adamük and Woinow (1871), and others. Adamük and Woinow found that the pupillo-constriction was not proportional to the distance of the point of fixation. Olbers (1780), on the other hand, had already shown that it was proportional to the angle of convergence, and E. H. Weber (1851) proved that constriction of the pupil occurred on convergence without accommodation, but not on accommodation without convergence; this can be shown by the use of prisms. Hering (1868) devised an experiment for showing that constriction of the pupil also occurs on accommodation without convergence, but Verwoort (1899) thinks that this was due to imperfect exclusion of convergence.

Adamük (1870) obtained depression of the eyes, strong convergence, and pupillo-constriction on stimulating the posterior part of the anterior colliculus in dogs and cats,

similarly convergence and pupillo-constriction from the floor of the aqueduct. These results were confirmed by Hensen and Völkers (1878), and the intimate association of the pupillo-constriction with the internal rectus was further demonstrated.

Henke (1860) put forward the view that the reverse effect, relaxation of accommodation for distance, was accompanied by active dilatation through the sympathetic. However this may be, Hensen and Völkers found that stimulation of the slightly more lateral sixth nucleus was accompanied by some pupillo-dilatation. This is probably an active pupillo-dilator *divergence synkinesis.*

Curious cases are on record in which pupillo-constriction accompanied outward movements of the eye (Adamük, Weiss, Sichel, v. Graefe, Schiff).

The Sensory Reflex is a dilator reflex induced by tactile, pathic and other sensory stimuli. It is a complex effect exhibiting a primary rapid dilatation due to augmentation of the dilator tone through the cervical sympathetic, followed by a second dilatation, rapid in onset but very slow in its disappearance, due to inhibition of the constrictor tone. When originated through spinal sensory nerves, the afferent impulses are carried up in the posterior columns of the cord.

In dealing with the course of the pupillo-dilator path we have seen that Chauveau (1861) first obtained the sensory reflex experimentally by stimulating the posterior columns of the cord. He found that if the cord was cut above the inferior cilio-spinal centre the effect was abolished, except in one experiment on an ass, in which a very small effect was produced. Claude Bernard (1862) showed that the sensory reflex might be obtained on stimulation of the central end of any sensory nerve.

Reference has already been made in the same section to the work of Salkowski (1867), Balogh (1869), Hurwitz (1878), Schiff and Foa (1875), François-Franck, Luchsinger, Bellarminow, and Braunstein. Balogh (1861), however, was

the first to obtain the sensory reflex after section of the ordinary dilator path in his experiment after excision of the superior cervical ganglion. Hurwitz, as we have seen, found that the effect was very slow after the cervical sympathetic had been cut. Vulpian (1878) observed reflex dilatation after removal of both the superior cervical and stellate ganglia. v. Bechterew (1883) contended that the sensory reflex was entirely due to inhibition of the light reflex, *i.e.*, of the tonic action of the third centre. He based this view largely upon the findings of neuro-pathology, the light and pain reflexes being almost invariably abolished together. He also supported it by further experiments. Thus, if one optic nerve is cut, no further dilatation was caused in the eye of that side by pathic stimuli unless the opposite eye was open, and contraction thereby excited consensually in the sphincter on the side of the lesion. Secondly, the dilatation was inconsiderable when the eyes were examined in a dim light. Thirdly, the degree of dilatation did not exceed that which followed the withdrawal of the light. These experiments were confirmed by Mayer and Pribram (1884), and later by Braunstein (1894). The last-named author found that after section of the third nerve inside the skull, stimulation of the central end of the sciatic nerve with strong and weak currents at periods varying from 12 days to 7 months after the operation caused no reflex movements of the pupil. He observed no change in the size of the pupil between the operation and the final experiment, though during the latter he obtained dilatation from stimulation of the cervical sympathetic.

The subject has received attention from this point of view recently by Anderson (1903). As the result of five experiments in which the pupillo-constrictor tract was divided in some part of its course, he found that well-marked dilatation could be obtained by stimulating the sciatic nerve, pinching the skin, or stroking the hairs. The effect was accompanied by all the usual effects of exciting the cervical sympathetic, and all were abolished if this was cut in addition to the third nerve.

The converse aspect of the subject has also been disputed. Luchsinger (1880) and Guillebeau and Luchsinger (1882) obtained the sensory reflex after the cervical cord had been cut above the inferior cilio-spinal centre. Kowalewski (1886) failed to obtain this result, and similarly Braunstein. Anderson obtained a positive result in the only experiment specially directed to the point; the effect was slow, and was accompanied by slight retraction of the nictitating membrane and eyelids. Second stimulation was ineffectual unless an interval of some minutes was allowed to elapse. The effect continued after destruction of the brain and medulla, and hence cannot have been due to inhibition of constrictor tone.

Anderson considers that the ordinary sensory reflex is of two-fold origin :—(1) reflex augmentation of the dilator tone, causing relatively rapid and short dilatation; (2) reflex inhibition of the constrictor tone, causing a second rapid dilatation which only slowly and gradually subsides.

Hippus.—Anderson makes a valuable contribution to the obscure question of hippus. He found that this occurred not uncommonly after section of the third nerve, but ceased immediately on cutting the sympathetic. It was excited by tactile stimulation, or by a certain state of anæsthetisation. It might be accompanied by rhythmic movements of the eyelids and nictitating membrane.

The Cerebral Synkinesis is also a complex phenomenon, and cannot be considered a simple reflex. It is induced by psychic stimuli, *e.g.*, fear, etc., and also by concentration of thought upon a bright light or a dark room. It is also largely an associated movement, accompanying eye movements which may be themselves due to sensory impulses.

The pure psychic reaction, entirely caused by ideas of light and shade, was described by Haab (1886), though Beer had long before discovered that he was himself able to alter the size of his pupils in this manner; it may account for some cases in which persons have apparently been able to alter their pupils at will. The phenomenon is unaccompanied

by any obvious movement of the eyes, and, therefore, cannot be called a synkinesis ; it is, in fact, a *psycho-kinesis.* The reaction has recently been called in question by Bumke (1903), and it must be admitted that it is very difficult to exclude the many sources of error, of which accommodation is the most probable and difficult to avoid.

I propose now to discuss in detail my observations on the relationship of the cerebral cortex to the movements of the pupil.

Fontana, as long ago as 1770, showed that in the cat, even under the strongest light stimulus, the pupils dilated widely if the animal was frightened by a loud noise. A child's pupil can also be made to dilate, even during ophthalmoscopic examination of the macula, by a loud sound, such as clapping of the hands. Raehlmann and Witkowski consider that psychic impulses assist in maintaining the tone of the dilator centre, accounting for the constriction of the pupil during sleep by their absence.

Schiff and Foa (1869) first stimulated the cerebrum by electricity, and obtained dilatation of the pupils from stimulation of the anterior four-fifths, and of the cerebellum only by strong stimuli. They attributed the effect to the sensibility of the brain.

Hitzig (1871) sometimes obtained constriction of both pupils, but generally dilatation, rarely only one pupil reacted.

Similar experiments have been carried out by Bochfontaine (1875), Danilewski (1876), Luciani and Tamburini, Grünhagen, Bessau, Ferrier, Horsley and Schäfer, Schäfer, Beevor and Horsley, Grünhagen and Cohn, Katschanowski, François-Franck and Pitres, Mislawski, Bechterew and Mislawski, and Braunstein. In most of these cases the observations were incidental during research directed to some other object. In all, dilatation was much more easily induced than constriction, and no accurate localisation was effected.

Most observers have regarded the effects as inconstant, and but little attention has been specially directed to them.

Thus Ferrier includes dilatation of the pupil with salivation from the submaxillary gland, changes in pulse and blood pressure, and "other indications of general reverberation throughout the organism." He regards them as "merely complications and not as results of localised cortical stimulation." On the other hand, Bechterew and Mislawski conclude that "stimulation of the given regions of the cortex and of the optic thalami has hit off the central endings (Verlangerungen) of the cervical sympathetic," and that "the chief reflex centre for the secretion of tears lies in the optic thalami, and that there, too, are found the central tracts of the cervical sympathetic, their prolongations (Fortsetzungen) being continued thence to the cortex." François-Franck is careful to distinguish between two causes of dilatation of the pupil resulting from cortical stimulation. One is a special and localised effect following excitation of definite foci in the cortex, and also obtained from excitation of the underlying fibres of the corona radiata and internal capsule. The other accompanies epileptoid convulsions resulting from stimulation of any and every part of the motor areas, and is never obtained from the underlying white matter, which does not induce the epileptic state. To the latter he attributes the dilatation after administration of curare which was observed by Bochfontaine. He perhaps lays too much stress upon this as a fundamental distinction, for it applies equally to other motor effects induced through the cortex.

My experiments were made principally upon cats; a few dogs and one monkey were also used. The animals were anæsthetised with ether, the degree of anæsthesia varying, but always being amply sufficient to cause insensitiveness to pain. The qualifying terms used apply to the condition of excitability of the motor areas of the cortex to stimuli of moderate severity, as shown by movements of the limbs of the contra-lateral side. "Epileptoid convulsions" is the term used to express the violent general movements which often follow stimulation of the motor area after exposure of

the brain to air, or prolonged or frequently repeated excitation. This condition is quite compatible with complete anæsthesia.

The cervical sympathetics were either cut or isolated on one or both sides. In the dog the vago-sympathetic was treated as a whole. This was also done in the cat to insure the complete division of all sympathetic fibres. In some experiments the superior cervical ganglion was extirpated to eliminate any dilator fibres which might reach the ganglion by any hitherto unknown course. Section of the sympathetic was usually followed by a distinct moderate constriction of the corresponding pupil, but this was certainly not invariably the case. Absence of a tonic dilator influence is probably under these circumstances due to the condition of anæsthesia of the animal.

I need not enter into further details of the operative procedures, which were those usually employed in cerebral physiology. It was important to keep the light falling upon the eyes as constant as possible throughout the experiment.

It is easy in the cat's eye to direct one's attention to the horizontal meridian. The constricted pupil being a vertical slit, the distance from the centre to the periphery can be divided into four imaginary parts, the pupil being said to be a quarter, a half, three-quarters, or fully dilated.

I have not paid much attention to any movements other than those of the eyes and pupils. Dilatation of the pupils is often obtained without any movement of the eyes or body. I have usually found that a slightly stronger stimulus is necessary to evoke it than that which is required to produce movement from excitation of the arm or leg areas; or the same strength of stimulus may suffice if the animal be slightly less under the influence of the anæsthetic.

(A) *Cat.*—In the cat dilatation of the pupil can be obtained from a considerable area in the neighbourhood of the crucial sulcus and from a considerable area of the occipital region. As the result of many experiments it is

found that the mesial surface of the hemisphere near the crucial sulcus (prorean and presplenial convolutions) gives the most marked effect, but I have also found that the anterior part of the third or median convolution (coronal or anterior supra-Sylvian) gives a very constant effect. In one or two instances there was a transitory constriction of the pupils before the dilatation from this area. Ferrier obtained constriction of the pupils and divergence of the eyeballs from this spot in the dog, but I have not observed the latter effect in the cat.

In the occipital region, what may be called the focal spot is in the posterior part of the third or median convolution (posterior supra-Sylvian convolution). I have not observed any constriction of the pupil here, as described by Ferrier. François-Franck, however, obtained a transitory constriction from this spot, followed by dilatation, exactly like that which I describe for the coronal gyrus. It is, therefore probable that there are foci for pupil constriction both in the frontal and occipital areas, but that they are masked by the dilator effects, which are much more readily produced. One may compare with this the greater representation of lateral eye movements over any other eye movements in the cortex.

Only the results which are deduced from a large number of carefully planned experiments can be considered trustworthy, more particularly in deciding between areas which give a positive result independently of epileptoid convulsions. These are very readily brought about by repeated excitation of the same or closely neighbouring areas, owing to the increased excitability of the cortex which is thereby induced. The condition of anæsthesia is also of the utmost importance. If this is deep, the pupils remain immobile. If it is too light, dilatation is obtained from almost every part of the cortex, at any rate when bodily movements occur. The results are only reliable when the anæsthesia is moderate.

(B) *Dog.*—The areas are very much the same in the dog as

in the cat. This animal is less suited for the purpose because of the rarity of dogs with light-coloured irides, and a round pupil is less easy to detect slight variations upon than the slit-like one of the cat. In the dog I obtained a very marked effect from the precrucial gyrus, but I failed to observe any convergence of the optic axes as noted by Ferrier.

(c) *Monkey.*—I have done only one experiment of this nature upon the monkey. I found it much the easiest animal to work with, and it gave very definite results.

We conclude, therefore, that previous section of the cervical sympathetic diminishes the effect, but by no means abolishes it. When both cervical sympathetics are intact, the dilatation of the pupil, when well marked, is accompanied by all the usual effects of excitation of the nerves themselves, viz., retraction of the nictitating membrane, widening of the palpebral aperture and projection of the eyeball; to these, Bechterew and Mislawski add secretion of the lacrymal gland, but this I am unable definitely to confirm. All these effects are abolished by previous section of the sympathetics except the dilatation of the pupils, and this is diminished. Whereas when the nerves are intact full dilatation of the pupils may occur, especially during epileptoid convulsions; after they are divided, the pupils rarely become more than three-fourths dilated. The effect is very well seen if one nerve is divided, the other being intact. In this case the two pupils move synchronously and apparently to the same extent, except that they start unequal, the one on the divided side being the smaller. François-Franck is, therefore, certainly wrong in asserting that the pupillary dilatation is unilateral if one sympathetic has been cut. He certainly admits a slight degree of dilatation, which he attributes to dilator fibres running another course, probably in the trigeminal. I have eliminated this possibility by dividing the fifth nerve intracranially, and still obtaining the undiminished effect. To eliminate the possibility of other dilator fibres reaching the superior cervical ganglion I have, as already stated, extirpated it. The pupil on the side from which the ganglion was

removed was slightly but appreciably smaller than on the side on which the vago-sympathetic was cut.

I have found that section of the third nerve intracranially after previous division of the cervical sympathetic causes the pupil to become immobile, about three-fourths dilated. Stimulation of the cortex has then no effect upon it.

Complete section of the corpus callosum has no effect upon the result of exciting the cortex. The bilateral effect is, therefore, not due to the stimulus acting through the opposite cortical areas, but to its acting upon lower centres, but whether the optic thalami or the superior colliculi, or the sub-collicular nuclei I am not prepared to say, but probably upon the last mentioned.

Stimulation of the anterior and posterior parts of the corona radiata and internal capsule containing the fibres derived from the cells of the frontal and occipital areas leads to bilateral dilatation of the pupils. I have generally found a stronger excitation necessary, but this may be due to the fact that stimulation took place at the end of prolonged experiments. In one case I obtained a very marked constriction of the pupils, with strong convergence of the eyeballs from stimulation of the posterior part of the internal capsule.

A point of great interest arising from these experiments is the question of the mechanism whereby dilatation of the pupils can occur in the absence of the usual dilator tract. Two explanations offer themselves, viz., inhibition of the tonic action of the third nuclei, and dilatation brought about by vascular changes in the iris. An extremely interesting observation by Sherrington may be mentioned in this connection. In bringing physiological experiment to bear upon current theories of the emotions, he performed "appropriate spinal and vagal transection" in the dog to eliminate "the sensation of all the viscera and muscles below the shoulder." He says:—"The eyes were well opened, and the pupil distinctly dilated in the paroxysm of anger. Since the brain had been, by transection, shut out from discharging impulses

viâ the cervical sympathetic, the dilatation of the pupil must have occurred by inhibition of the action of the oculo-motor centre."

It is said that after the optic nerves have been cut, dilatation of the pupil is not obtained upon section of the third nerve, and hence tonic action of the third nuclei has sometimes been denied. There can be no question, however, that it exists when the optic nerves are intact, as in my experiments.

The immobility which follows section of both the third and the sympathetic is strong evidence in favour of the inhibition theory. It must be noted, however, that the blood pressure was probably very low at this stage of the experiment.

We have seen that dilatation of the pupil is still obtained after section of the sympathetic. No vaso-motor fibres are known to run to the iris, except by way of the sympathetic, and even if such exist, the experiments of Langley and Anderson tend to show that vascular effects are inefficient to bring about the dilatation observed. Moreover, it is well known that changes in blood pressure may occur from stimulation of various parts of the cortex, whereas pupil dilatation only occurs from certain localised spots in the absence of the epileptoid state.

It seems justifiable from these considerations to regard the effect as another example of direct inhibition of the oculo-motor nerves from the cortex.

There is no lack of evidence as to the presence of fibres connecting the cortex with the mesencephalon, and some of these must be regarded as the ones concerned in the pupillary effects. We may leave out of the question the dilatation of the pupil which accompanies the epileptoid state, for this is undoubtedly of an extremely complex nature, requiring special investigation. Confining our attention to the more specialised results obtained from the oculo-motor area in the posterior part of the frontal convolutions, which are to be looked upon as part of the fronto-parietal motor or kinæsthetic

area and quite distinct from the more anterior or so-called pre-frontal area, and to the results obtained from the oculo-sensory or visual area in the occipital convolutions, we find definite anatomical connections with the lower centres.

The pallio-tectal or cortico-mesencephalic system of fibres has recently been thoroughly investigated by Dr. Beevor and Sir Victor Horsley. It is noteworthy that no fibres were found passing to the mesencephalon from the frontal region, *i.e.*, from the area of cortex in front of the excitable cortex. From lesions of this part there was marked degeneration of the fronto-thalamic fibres previously described by Déjerine; the only mesencephalic centre to which fibres could be traced was the upper or anterior part of the locus niger. No fibres, therefore, go to the tectum.

A large number of fibres could be traced from the excitable cortex to the corpora quadrigemina and mesencephalon, especially to the superior colliculus. This was very marked in the cat, much less so in the monkey. The fibres from the oculo-motor areas have not yet been specially investigated.

The results from lesions of the occipital lobes were particularly striking, and confirmed Edinger's researches on birds. In proportion as more of the area of the cortex containing Gennari's streak is involved in the lesion the number of degenerated fibres passing to the colliculus increases. The fibres are large, and stand out distinctly from the medium-sized occipito-thalamic and occipito-geniculate fibres, and from the small callosal fibres and fine collaterals which enter the corona radiata in large numbers. Some of the occipito-tectal fibres pass among the fibres of Gratiolet's radiation, others run through the mesial region of the inferior longitudinal bundle. All the fibres are distributed to the whole breadth of the stratum griseum profundum of the superior colliculus.

Which of these fibres are concerned in the pupillary phenomena, and whether they pass, any of them, directly to the superior pupillo-dilator centre or to the pupillo-

constrictor centre, or only by intermediate connections, must be left for future research to determine. We have already shown that the cortical pupillo-dilatation is a complex event, strikingly resembling the ordinary sensory dilator reflex in that it is accompanied by all the usual effects of stimulation of the cervical sympathetic as long as that path is intact, but that it also occurs, deprived of the other sympathetic effects, when this nerve is divided. The evidence is, therefore, in favour of a more circuitous course, or at any rate of multiple and complicated interconnections.

There is evidence that pupillo-constriction can also be elicited from stimulation of the cortex. Ferrier obtained it from stimulation of the anterior and posterior limbs of the angular gyrus in the monkey, but this observation is probably incorrect. I have already stated that, apart from a transitory constriction (*cf.* François-Franck and Pitres), I failed to confirm the same observer's results from the third external or coronal convolution in dogs. In pigeons, Ferrier found intense constriction of the pupil from excitation of the middle of the convexity of the hemisphere. Schäfer obtained marked constriction of the pupil from stimulation of the quadrate lobule in monkeys.

This brings us to the consideration of the exact nature of the phenomena. The view of Bechterew and Mislawski that we have here the central prolongations of the cervical sympathetic, is, *a priori*, highly improbable, or at any rate a misleading explanation of the results. Indeed, the continuance of the dilatation after section of the cervical sympathetic proves that it can only be partially true.

So, too, it is unlikely that we are dealing with "centres" for the pupils, in the ordinary sense of the term. We have found that the effect is most specifically obtained from the areas which are most concerned with ocular movements, whether from the motor or the sensory side. Moreover, it would seem that the effect is indissolubly connected with those movements, and does not occur in their absence Hence it is most reasonable to conclude that the phe-

nomenon is an associated effect. As regards the so-called sensory areas, *i.e.*, the visual centres in the occipital cortex, it is probable that the attention plays some part. We produce, by artificial excitation, some strong, but probably ill-defined, visual sensation, which arouses the attention, and leads to the appropriate movement of the head and eyes towards the direction from which the stimulus seems to proceed. The sensation is strong and sudden, and is accompanied by dilatation of the pupils in no physiological sense other than the expression of emotion.

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THROMBOSIS OF THE CENTRAL VEIN OF THE RETINA.

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The ophthalmoscopic condition known as "thrombosis of the central vein" is a sufficiently well recognised one. There are indeed certain borderland cases in which, although there are copious retinal hæmorrhages, one hesitates to make a definite statement because the signs of venous obstruction which are of primary importance in the diagnosis, are insufficiently marked. Yet there is usually but little difficulty in separating this from other hæmorrhagic conditions of the retina, and it may justifiably be given a place as a clinical entity. The object of the present paper, however, is to discuss the subject not from the clinical, but from the pathological point of view, on the basis of four cases which I have recently had the opportunity of examining microscopically,—to discuss in fact the question, "what is the pathological basis of the accepted clinical picture"?

Arguing merely from the clinical standpoint, when one sees the large hæmorrhages and the enormously swollen and tortuous veins, at one place buried in exudation, at another thrusting forth a knuckle, one is driven to the assumption that there must be something obstructing the venous return; and when one further finds that these appearances are usually confined to one eye, the other fundus being either normal or showing only slight vascular disease, while there is no proptosis or other evidence of obstruction of the ophthalmic vein, the conclusion seems inevitable that the obstruction must be in the central vein of that eye and not anywhere farther back. Arguing further *a priori* we find that these cases occur usually in elderly people, that in the form of thickened peripheral vessels and cardiac hypertrophy, there are often

signs of wide-spread vascular disease, and that in a certain proportion of instances there is evidence of nephritis. All these are conditions which tend to favour vascular obstruction, and which cases are indeed known to cause obstruction in the cerebral vessels ; hence it seems probable that in the case with which we are dealing, the obstruction in the central vein will be a thickening of the vein wall, or a thrombus within its lumen, or a combination of these two conditions. When now we find that loss of vision is usually sudden, or at least not very gradual, and that there are usually not any definite prodromal symptoms, it might be concluded that the occurrence of a thrombosis and not of a very gradually built-up thickening of the vein wall would most probably be the immediate cause of the loss of vision. Sclerosis of the vein wall would of course predispose to such a process of thrombosis.

We see, therefore, that the thrombus in the central vein which is commonly assumed to be present in these cases would theoretically account well for the clinical signs and symptoms, but when we turn to those recorded cases in which a pathological examination has been carried out, in order to find how far such theorising can be substantiated, we see that while a thrombus has indeed been discovered in a certain number of the cases, it has not been found in all. It is not necessary to introduce a discussion of all the literature into my text. This has been done frequently by different authors, and recently and sufficiently fully by Ischreyt. It will be useful, however, for ease of reference on special points, and because it seems not to have been done before, to briefly tabulate those cases from the literature in which a sufficiently full pathological examination has been made of the cases under consideration. I have omitted from the list two cases which Angelucci* reported as "thrombosis of the central vein," because it is practically certain that they were not of this nature. They occurred in young persons, there were no retinal hæmorrhages and but

* Angelucci, Klin. Monatsbl. f. Aug., 1878, p. 443, ditto 1879, p. 151, ditto 1880, p. 21.

moderately dilated veins, the clinical history resembled that of embolism of the central artery, and indeed they both had aortic valvular disease. Michel,* who had the opportunity of examining Angelucci's specimens has recently stated his conviction that the appearances in his first case were due to a psammoma-like concretion lying outside the vein, and perhaps compressing the artery, while in his second case they were due to *post-mortem* coagula. Indeed, Angelucci reports a third case (which was not examined pathologically) in which there was retinal œdema, and the cherry-red spot at the macula, and includes these two as signs of thrombosis of the central vein! I have also excluded some cases in which a thrombus was mentioned, but in which insufficient details are given. A case of Juler's† for instance, a man of 39 who suffered from heart-disease, and had hæmorrhagic retinitis and glaucoma, in whose eye a "clot of a central vessel" was found. Also a case of hæmorrhagic glaucoma mentioned by Schnabel‡ in which he found "cellular infiltration round the vein and thrombosis of it."

It is also to be remarked that some of the cases included in the list are not altogether convincing. Michel seems to be not quite sure whether his own first case may not have been an obliteration of the vein by proliferation of the intima rather than a true thrombosis; the picture given of his second case rather suggests a leukæmic blood-clot with abundant leucocytes, while the picture of his third case also resembles a coagulum deposited from stagnant blood rather than a true *intra vitam* thrombus, *i.e.*, it shows neither the lamination of a recent thrombus nor the organisation of an old one. Similar appearances are not uncommon in the ciliary vessels and are noted in Case III below. The same remarks apply to Gauthier's case, and to Fridenberg's, and probably also to Würdemann's in which a "clot" is spoken of in both the artery and vein. In Meyerhof's case it is also doubtful

* Michel, Zeitsch. f. Augenh., pt. 2, 1899, p. 28.
† Juler, Brit. Med. Journ., 1896, September, p. 811.
‡ Schnabel, Arch. f. Angenh., vol. xxiv, p. 283, 1892.

Author.	Sex and age.	Albuminuria.	Evidence of vascular disease.	Clinical history.	Pathological examination.
1. Michel, 1878, Arch. f. Ophth., vol. xxiv, pt. 2, p. 37.	M., 53	None ..	General arteriosclerosis, threatening of hemiplegia. *P.M.* Cardiac hypertrophy and mitral insufficiency.	Usual picture of "thrombosis of central vein" observed for 16 months without any great change. Eye obtained *post-mortem*.	Cellular thrombus 1½ mm. long, 6 mm. from eyeball. Distended perivascular lympth-sheath and round-celled infiltration. Artery, thickened adventitia. Organised blood in vitreous.
2. Michel, 1878, Deutsch. Arch. f. Klin. Med., p. 306.	?	?	?	Retinal hæmorrhages found *post-mortem* in a case of leukæmia.	Thrombus (molecular detritus, round cells and red blood corp.), 1½ mm. long at point of exit of vein from optic nerve.
3. Michel, 1899, Zeitsch. f. Aug., vol. ii, p. 1.	F., 37	Present ..	General arteriosclerosis, hypertrophy of left ventricle.	"Retinitis albuminurica" both.	Thrombus in left central vein; homogeneous periphery, granular centre. Thought to be of 3—8 days' duration. Coagula in retinal veins. Retinal arteries thickened.
4. Deutschmann, 1879, Arch. f. Ophth., vol. xxxv, pt. 3, p. 163.	M., 72	?	?	Hgic. retinitis R.; veins tortuous. Glaucoma 9 months later. V. L. 6/12. O.E. normal.	No thrombus; hges. into optic nerves; central vessels normal. Corneo-iritic angle closed.
	M., 54	?	?	Hgic. retinitis R.; glaucoma 9 months later.	No thrombus; hyaline thickening of retinal vessel walls giving the amyloid reaction. Corneo-iritic < closed.

Author.	Sex and age.	Albuminuria.	Evidence of vascular disease.	Clinical history.	Pathological examination.
5. Wagenmann, 1892, Arch. f. Ophth., vol. xxxviii, pt. 3, p. 213.	M., 66	None ..	Arteriosclerosis cardiac hypertrophy.	Hgic. retinitis R. coming on in the night; glaucoma 1 month, and excision 3 months later. L. normal.	No thrombus; endarteritis in central artery and ? multiple emboli in retinal arteries. Very little change in veins. A.C. < closed.
	M., 76	Trace ..	Arteriosclerosis; three attacks of agraphia.	Hgic. retinitis; 7 months later glaucoma and corneal ulcer; 1 year after onset, enucleation. V. L. 6/6.	Thrombus; finely granular mass without nuclei projecting half-way into lumen of vein, remaining space being filled with blood. Veins and arteries both thick-walled and with proliferation of intima. A.C. < closed.
	M., 42	None ..	None	Hgic. retinitis R. L. normal. 4 months later iritis with post. synechiæ and glaucoma. Excision 5 months from onset.	No thrombus. Retinal vessels much thickened; endothelial proliferation; sometimes quite closed. Hyaline degeneration. Inflammatory foci A.C. < blocked.
6. Weinbaum, 1892, Arch. f. Ophth., vol. xxxviii, pt. 3, p. 191.	M., 26	None ..	None	Sudden D.V. of R.; 2 months later, when first seen, glaucoma and hgic. retinitis. Iridectomy followed by hge. Excision 14 months after onset. V. L. = 6/6. O.E. normal.	Thrombus $\frac{3}{4}$ mm. long, $1\frac{1}{2}$ mm. behind lamina cribrosa. Scaffolding of fibres and spindle-cells with some nests of round-cells between. Cleft between it and wall filled with blood. Vein elsewhere of normal lumen. A.C. < closed.

7. Purtscher, 1896, Arch. f. Augenh. Ergänzungsheft, p. 1.	F., 21	None ..	Liable to epistaxis.	D.V. R. 2 months. Glaucoma when first seen. Excision 3 months after onset. Hgic. retinitis found on bisecting eye. L. retinitis proliferans and hges.	Thrombus 0·6 mm. long central to lamina; organising, leaving a little space at one side. Retinal vessels hyaline; new-formed tissue in vitreous. A.C. < closed.
8. Stölting, 1897, Arch. f. Ophth., vol. xliii, pt. 2, p. 306.	F., 65	None ..	Cardiac irregularity. No rigidity of peripheral vessels.	Hgic. retinitis R.; 1 month later glaucoma. Iridectomy. Excision 3 months from onset. V. L. 4/6.	No thrombus. Narrowing of both artery and vein at lamina. Hyaline degeneration of retinal vessels. A.C. < not closed.
9. Goh, 1897, Arch. f. Ophth., vol. xliii, pt. 1, p. 147.	M., 25	Tube-casts	None	Hgic. retinitis on both sides 3 days before death from stomatitis gangrænosa and septicæmia. Veins enlarged and tortuous. Many new hges. before death.	R. Recent marantic thrombus 1 mm. behind lamina, leaving a small lumen at one side. Retinal vessels normal, but distended. L. No thrombus in central vessels; thrombi in smallest retinal vessels.
10. Alt, 1897, Amer. Journ. Ophth., p. 114.	F., 64	Doubtful trace	None	D.V. R. 3 weeks. Large macular and many small hges. Vessels dark and tortuous. 4 weeks later glaucoma; more retinal hges. hyphæma. Excision 2 weeks later. L. V. = 20/100. 3 D. Hm.	"Thrombosis and thrombophlebitis" of larger retinal veins and "pigmentary degeneration" of smaller. Central vessels not described. A.C. < shut off.

Author.	Sex and age.	Albuminuria.	Evidence of vascular disease.	Clinical history.	Pathological examination.
11. Fridenberg, 1897, Arch. f. Aug., vol. xxxiv. p. 175.	M., 70	Albumen and tube-casts	?	Hgic. retinitis and glaucoma. D.V. had lasted 1 year, but 1½ years before its onset a small retinal hge. had been accidentally found on testing for glasses. Iridectomy, but 3 weeks later hyphæma and high tension. Excision.	"Hyaline thrombi" in many vessels, especially on the disc. Walls of central and retinal veins normal. Hyaline degeneration and proliferation of intima in arteries. A.C. < blocked.
12. Bankwitz, 1898, Arch. f. Ophth., vol. xlv, pt. 2, p. 384.	F., 72	?	Arteriosclerosis. Several apoplectic strokes. Right hemiplegia.	Hgic. retinitis. D.V. R. (first noticed on awaking) of 5 weeks' duration. Later glaucoma, iritis, posterior synechiæ. Excision 2 months after onset. L. cataract incip. O.E. normal. V. = 6/18.	Small aneurism on artery in front of lamina supposed to have obstructed vein and caused thrombosis of it. Retinal arteries much thickened, in places obliterated. Veins also thick, some containing thrombi, others crammed with blood.
13. Türck, 1898, Deutschm. Beitr. z. Augenh., Heft. xxiv, p. 45.	M., 67	None ..	Cardiac irregularity. Endocarditis *P.M.*	Hgic. retinitis L. D.V. 4 weeks previously. Patient died 9 days later. No glaucoma. R. with −0·5 D. sph. = 6/12. Incipient cataract.	Organising thrombus, 1 mm. long, just behind lamina. Fully fills vein in front, leaves clefts behind. Vessel walls normal in nerve, slight thickenings in retina. A.C. < blocked.

14. Würdemann, 1898, Deutschm. Beitr. z. Aug., Heft. xxix, p. 100.	M., 8	None ..	None	Hgic. retinitis L. coming on 14 days after mumps (patient seemed quite recovered). 1 year later acute glaucoma; excision. V. R. 6/6 normal.	"Clot" in artery from 1 mm. behind lamina backwards for 5 mm.; small clot in vein not completely occluding lumen. New-formed tissue in vitreous. A.C. < closed.
15. Reimar, 1899, Arch. f. Aug., vol. xxxviii, p. 209.	F., 57	None ..	General arterio-sclerosis.	Hgic. retinitis with greatly tortuous veins of 5—6 weeks' duration. 8 months later glaucoma; slight iritis. Sclerotomy unsuccessful. Excision.	No thrombus. Veins partly normal, partly much thickened. Endarteritis in central and retinal arteries, and some small miliary aneurisms in latter. Vitreous hæmorrhage. A.C. < closed.
16. Gauthier, 1898, Annales d'oculistique, vol. cxix, p. 438.	M., 45	None ..	?	First seen with iritis R. Glaucoma followed, for which sclerotomy and iridectomy done, and fundus now first visible showed hges. Glaucoma reappeared. Excision.	Central vein contained hyaline mass extending from lamina into main branches. Lumen completely obstructed in some places, partly in others. Iris adherent to lens. A.C. < not mentioned.
17. Meyerhof, 1900, Zeitsch. f. Augenh., pt. 4, p. 676.	M., 50	None ..	Slight arterio-sclerosis; systolic murmur.	L. Hgic. retinitis. R.V. 6/6. 9 years later glaucoma L.; iridectomy; relief. Again glaucoma, 1 year later. Excision. V. R. still 6/6, but later some hges.	Central vessels normal; in retina thickening of media and adventitia Dark red masses in lumina ? thrombi of both arteries and veins.

Author.	Sex and age.	Albuminuria.	Evidence of vascular disease.	Clinical history.	Pathological examination.
18. Ischreyt, 1900, Arch. f. Augenh., vol. xli, p. 38.	M., ?	None ..	General arteriosclerosis.	1st symptom = scotoma before R.; not examined at time. 2 months later glaucoma and fundus invisible. Excision. Copious hges. in every part of retina. V. L. with −4 sph. = 6/12. O.E. normal.	Thrombi in super. and infer. nasal veins and walls thick and hyaline. Central vein normal. Endarteritis of central and retinal arteries, and hyaline thickening of retinal. A.C. < closed.
19. Yamaguchi, 1903, Klin. f. Aug. Beilageheft, p. 180.	M., 25	?	None	Signs of cerebral tumour. Optic neuritis going on to atrophy. 1 year later recurrence of choked disc with many retinal hges. Typical picture of thrombosis of central vein. Obtained *P.M.*	While crossing the vaginal space vein narrowed by contraction of cicatricial tissue. Thrombotic masses lying against wall. No endothelial proliferation, but wall hyaline.

whether we are dealing with true thrombi or with coagula. Bankwitz's explanation of an aneurism on the artery obstructing the vein sounds improbable, while Goh's case belongs to a somewhat different category from those under consideration, since it occurred during an exhausting illness and only a few days before death.

Shortly to summarise the different pathological changes which have been put forward in explanation of the clinical picture of "thrombosis of the central vein" we have: (1) A thrombus in the central vein in 11 out of 22 cases; (2) Occlusion of the central vein by proliferation of the intima, but without thrombosis (possibly in Michel's first case); (3) Multiple thrombi in the retinal veins, but without a thrombus in the central vein (Alt, Ischreyt); (4) Multiple emboli, or perhaps thrombi in the retinal arteries (Wagenmann, Case I).* Stölting seems to regard his case as of the same sort. In Fridenberg's and Meyerhof's cases there were thrombi (or coagula) in both the arteries and veins; (5) Changes in the retinal vessels (hyaline thickening, endarteritis, endophlebitis) sometimes amounting to occlusion, but not the result of either thrombosis or embolism (Wagenmann, Case III, Deutschmann, Case II, Reimar); (6) Hæmorrhage into the substance of the optic nerve (Deutschmann, Case I).

No remarks are needed on the first three of these explanations, since it is sufficiently obvious how the ophthalmoscopic appearances might be produced by them. With regard to No. 5 also there is no insuperable difficulty in accounting for the clinical picture if we suppose the thickening to fall chiefly on the vein walls and to produce obstruction of the venous current. It is not so plain, however, why lesions on the arterial side of the circulation, whether emboli, thrombi, or endarteritis, should give rise to the appearances of venous obstruction and to the copious hæmorrhages. The explanation usually given is that we are really dealing with multiple

* Wagenmann at first regarded the lesions as multiple emboli of the arteries, but has recently (Sitzungsbericht der Ophth. Gesellsch. z. Heidelberg, 1898, p. 251) given his opinion that they may have been thrombi.

hæmorrhagic infarcts such as occur when the pulmonary or any end artery is blocked, *i.e.*, that when an obstruction occurs in an artery to which there are no sufficient collaterals, and when in consequence the blood-flow through the corresponding vein is stopped, there occurs a back flow of venous blood in a direction the reverse of the usual, which causes engorgement of the vein and hæmorrhages from it. A case of Knapp's* is usually quoted in which the ophthalmoscopic appearances seemed to indicate that there had occurred an embolism of a single arterial branch in the retina, and in which the corresponding vein was engorged and accompanied by hæmorrhages. Haab,† however, has suggested that the real explanation of this case was that a thrombus in the vein had been the primary lesion, and that in consequence of the obstruction to the blood-flow an endarteritis had been set up in the artery, which gave it the thin appearance of an artery in which an embolus had lodged. It has been abundantly proved, and is indeed a matter of common experience, that branch embolism, like embolism of the main trunk, is not usually followed by any such hæmorrhages as those described in Knapp's case. Haab‡ quotes 20 authorities in support of this statement, and in three cases of branch embolism personally observed I never saw any trace of hæmorrhage. It must therefore be considered doubtful whether obstructions on the arterial side of the circulation do offer any explanation of the ophthalmoscopic appearances in these cases. Deutschmann's finding of hæmorrhages in the optic nerve as a cause of "thrombosis of the central vein" has, so far as I know, never been repeated. The frequency of the occurrence of glaucoma in the cases tabulated may be merely noticed at present. I shall return to this point later.

Certain questions arise on studying these results. Is the clinical picture known as "thrombosis of the central vein" capable of being produced by more than one kind of

* Knapp, Arch. f. Augenh., vol. i, p. 29, 1869.

† Haab, System of Dis. of the Eye, Norris and Oliver, vol. iv, p. 519.

‡ Haab, *ibid.*, p. 505.

lesion, as is suggested by the variety of the findings in the above list? If so, have we any means of distinguishing clinically what lesion is present in any given case? If not, if there is some constant pathological entity as the basis of the well-defined clinical entity, how can we reconcile the variety in the pathological explanations which have been brought forward in different cases? It must be said that these questions cannot yet be answered with any degree of certainty, and though it is now 26 years since Michel published the first case, there is still need for the collection of fresh material, for it is only by having at our disposal a large number of reports, so far as possible clinical as well as pathological, that we can hope to come to a final conclusion. We find in the literature more than one case in which all the appearances clinically pointed to venous obstruction, and yet on pathological examination no thrombus or other impediment was found in the veins. It is possible that in some of these cases there really was an obstruction to the vein, which was overlooked in the pathological examination. Such a possibility exists, of course, where the whole length of the vein has not been examined in serial section, and in order that no part may be overlooked it is always desirable that the optic nerve entrance should also be cut in *transverse* serial section, and not horizontally in the usual manner. It is notoriously difficult to speak with certainty as to whether the lumen of a vessel is free or occluded, and as to whether its walls are thickened or not, when the vessel is cut longitudinally, for if the section does not happen to travel exactly up the centre of the lumen without any obliquity it is almost impossible to be sure of the condition of the vessel wall, and more especially is this the case when the vessel is collapsed and folded. A study of the literature and of the cases recorded below will show that the favourite seat for the lodgment of thrombi is either at the lamina cribrosa or a short distance behind it, probably because (Hertel), the central vessels narrow as they go through. The place where the central vein makes its exit from the nerve is also stated

by Michel to be a favourite seat, from the obliquity of the course of the vessel in this position, but a case of his own (No. 2 above) and one of Yamaguchi's (No. 19) seem to be the only ones on record of thrombus in this position. It may, therefore, easily happen that a thrombus may be overlooked, on the one hand at the lamina because the sections have been longitudinal to the nerve, and on the other hand at the exit of the vein from the nerve if this point be not included in the piece of nerve excised.

There is a further difficulty in the interpretation of the pathological appearances in some of these cases. In many of them the initial lesion occurred long before the eye came to excision, and during part of that time glaucoma was present. It becomes difficult to say, therefore, what changes were primary and what secondary, for it is likely that in an eye long the subject of glaucoma, interference with the intraocular circulation will itself give rise to vascular changes and even to thrombosis in the retinal veins, and though it is improbable that increased intraocular tension should give rise to a thrombosis in the central vein behind the lamina, yet even this is possible as a result of slowing of the intraocular circulation. Then, again, it does not follow in every case of glaucoma in which on bisecting the eye retinal hæmorrhages are found, that these hæmorrhages have preceded the onset of glaucoma, as is the usual history in true cases of thrombosis of the central vein. For in any glaucomatous eye in which the vessels are extensively diseased, hæmorrhages will be liable to occur, and more especially will this be the case if the tension have been suddenly relieved by opening the anterior chamber for the performance of an iridectomy or sclerotomy. Analogous cases are furnished by the hæmorrhages which sometimes ensue on too quickly and completely withdrawing fluid from the pleural cavity, or from a much over-distended bladder. It is necessary, therefore, in each case, unless it is known from actual observation that the retinal hæmorrhages preceded the glaucoma, to weigh the clinical with the pathological evidence before coming to a conclusion with regard to the sequence of events. If a history be given of

sudden loss of vision in the form of clouds and mist before the eyes, perhaps noticed on waking in the morning, if there have been at first no pain or redness of the eyeball, but if these symptoms have made their appearance later, then the probability is strong that the case was indeed first one of thrombosis of the central vein upon which glaucoma ensued. If, on the other hand, the history be of loss of vision with supraorbital neuralgia, pericorneal redness and rainbows round lights, then it is probable that the glaucoma was the first fact and that the hæmorrhages ensued later, either as a consequence of vascular disease or as a result of operative interference.

The following, then, are desirable conditions in the material upon which we conduct our investigations on thrombosis of the central vein. The disease should not have lasted too long, otherwise it will be difficult to separate primary from secondary lesions. Glaucoma should not have been present, since it complicates matters, or if it has been present (for we seldom obtain pathological material in which it has not occurred), it should not have lasted long enough to mask the earlier condition of affairs. It should be known by actual observation, or rendered probable by the history of the case, that the hæmorrhagic retinitis and not the glaucoma was the first factor in the case. The eye should not have been too much interfered with by operation. The eye should be cut in serial section, and more especially the disc and lamina cribrosa should be cut in transverse serial section. All these conditions are seldom fulfilled in one case, but some of them were present in Case 1 to which we may now pass.

Case I.

Mrs. S., æt. 45, a cook, was admitted to the R.L.O.H. on 15.vi.03, under Mr. Treacher Collins. She was a very stout woman, and somewhat breathless on exertion, but, except for gall-stones 15 years before, she had never had any serious illness, and she believed herself to be in perfect health. She was accustomed to work in a rather hot place, and had to do a

good deal of stooping, but her work did not subject her to any great physical exertions.

Four days before her admission—on the afternoon of June 11th—while she was sitting quietly and reading a book, there came a sudden mistiness over the sight of the right eye, on account of which she kept rubbing her spectacles. This increased in density until, by next morning, she was practically blind in that eye. Since then there had been some movements in the clouds before the eye, but vision had remained in the same state.

The pulse numbered 62, and was regular; the radial and superficial temporal arteries were not appreciably rigid. No abnormality was detected in the heart or lungs, though auscultation was difficult on account of her stoutness. The urine was acid. Sp. gr. 1007. Abundant albumen. No sugar.

The right pupil reacted consensually, but not directly, the left normally. The external appearance of the eyes was otherwise normal.

V.R. = shadows. V.L. 6/12, with − 0·5 cyl. Ax. H. = 6/6 letters. O.E.R. The disc was congested and hazy; no definite margin was visible, and, in the surrounding retina, there were large masses of exudation spreading out on all sides, but roughly following the lines of the main vessels. The arteries were often invisible, but, where seen, were apparently of about the normal calibre. The veins were greatly enlarged, and very tortuous and dark, especially one proceeding upwards. They were often entirely buried in exudation, while here and there a tortuous knuckle looked through. On the disc they were for the most part invisible. Scattered everywhere throughout the fundus there were innumerable hæmorrhages, small and large, striate, rounded, and irregular. The disc was but little, if at all, swollen above the level of the surrounding retina.

O.E.L. The relations of the veins to the arteries was normal, and there were no vascular changes or hæmorrhages. The disc was normal. There were a few sharply-defined, glistening yellow specks to the nasal side of the disc, which were believed to be outgrowths of the lamina vitrea.

She was seen again on June 22nd, when the ophthalmoscopic appearances were unaltered.

24.vi.03. She was admitted with glaucoma. T + 1. Cornea

a little steamy. Pericorneal congestion. Anterior chamber *deep*. Pupil semi-dilated and fixed. The media were too opaque to allow of any examination of the fundus, but, knowing of the presence of retinal hæmorrhages and of the exceedingly bad prognosis for operative interference in these cases, Mr. Collins decided merely to paracentese the anterior chamber, and not to attempt an iridectomy or sclerotomy in the first place. This was accordingly done, and the aqueous was let off as slowly as possible (the patient was very restive), yet a minute stream of hæmorrhage was seen to come from two places in the iris.

This operation relieved the tension at the time, but the patient became very ill, took suppression of urine, and died on July 1st. The eye was obtained *post-mortem*, but a full autopsy was not performed. The globe was hardened in 10-per-cent. formol, and bisected horizontally.

Macroscopic Examination.—The anterior chamber was of good depth. It contained no blood, and the angles did not look blocked. The retina was strewn with hæmorrhages, but there were none in the vitreous.

Microscopic Examination.—The optic nerve was shaved off close to the globe, and cut in serial section, every 5th section being mounted. The globe itself was cut in serial section, every 10th section being mounted until the edge of the disc was reached, when every 5th and in the centre all the sections were prepared. The piece of nerve remaining with the eyeball was unfortunately cut longitudinally.

Cornea.—Normal.

Corneo-iritic Angle.—On the temporal side, the iris is adherent to the extent of about one-half of the ligamentum pectinatum. It is a true adhesion, and not a mere apposition of iris and ligamentum, since new formed fibrous tissue can be seen crossing from the one to the other, and it is not torn in any of the sections. It nowhere reaches as far as the membrane of Descemet, and the ligamentum pectinatum preserves its usual spongy texture, and seems as if drainage could still go on well through it. There is a good deal of brown granular pigment among the trabeculæ, and this reaches forward a little distance between the membrane of Descemet and the deepest layers of the corneal stroma. In a few sections there are some blood

corpuscles in the spaces of Fontana. The canal of Schlemm is normal, and contains no blood. On the nasal side the blocking is very slight, and is probably more an apposition than a true occlusion. The angle is never rounded, but the connection of iris and ligamentum pectinatum by fibrous tissue is lacking. There is some homogeneous coagulum in the anterior chamber at the angle.

Iris.—The iris stroma is normal. There are no inflammatory foci in it, but near the root there are a few small hæmorrhages. Some of the vessels show very great thickening of their walls, even taking into account that the iris vessels are normally thick-walled for their size. Both the endothelium and outer coats are affected; we have most internally a layer, three or four cells deep, of well-stained ovoid nuclei surrounding a very narrow lumen; then comes a broad, almost homogeneous, layer, taking on the eosin staining but little, and showing only a very few elongated nuclei; outside of this, again, the pigment cells of the iris stroma are arranged so as to form an outer ring. These changes are best marked near the root of the iris on the adherent side, they are only slightly present on the non-adherent side, and in the smaller vessels near the pupillary margin. They sometimes cause total obliteration of the vessel concerned.

Ciliary Body and Choroid.—The ciliary muscle is normal. There are some hyaline-looking masses in some of the processes. The circulus major shows no endarteritis, but there are some small sclerosed vessels near the root of the iris. In the choroid there are hyaline outgrowths of the membrane of Bruch, which are mostly small, but some of which project through the pigment epithelium. The choroidal vessels are normal; some of them have a great many leucocytes within their lumina, and this is especially so on the temporal side.

Retina.—The retina shows the changes usual in hæmorrhagic "retinitis," no true inflammatory appearances, but merely distortion from the out-pouring of blood among its layers. The hæmorrhages are very abundant, but not usually of large size, so that the retinal layers are fairly well preserved. They are present for the most part in the inner layers, but sometimes extend through the outer nuclear layer, and are occasionally sub-retinal. There is no sign of their having broken through

the membrana limitans interna, and there is no blood in the vitreous. They are largest near the disc and become smaller in the periphery. Between the outer granular and outer nuclear layers there are some homogeneous coagula and fibrinous masses of small size. The retina near the ora serrata is vacuolated; the pars ciliaris normal.

Retinal and Central Vessels.—These showed the changes of most importance in the case. For convenience they will be taken together, and both arteries and veins will be traced backwards from the retina through the nerve. Much assistance was afforded in the study of the changes in these vessels by the use of Weigert's elastic tissue stain, which greatly helps in the case of the retinal vessels in distinguishing arteries from veins, since there seems to be no elastic tissue in the walls of the latter. In the case of the central vessels it picks out the elastica interna of the artery, and shows very beautifully the presence and extent of any endarteritis which may be present. The *retinal arteries* then show a very marked thickening of their walls, which causes great narrowing of their lumina, usually in an eccentric manner (fig. 1). As is shown by Weigert's stain, it is entirely within the elastica interna, and consists, therefore, of a proliferation of the intima. The cells composing it are large, with a clear, and sometimes with a vacuolated, cell-substance, and there is usually a well-preserved endothelial lining towards the lumen. These changes are most marked in the larger vessels near the disc, but are also present far out into the periphery. As it comes through the lamina cribrosa the artery has a good clear lumen and shows but little sign of endarteritis. Farther back there is again more endarteritis, which Weigert's stain resolves into a large number of curly fibres within the true elastica, some quite small and fine, others larger and coarser, and forming as it were little pieces of elastic membrane within the membrane of Henle proper, each reaching a little way round the lumen, but none completely round. Among these curly fibres the nuclei of the intima are to be seen.* This condition of the artery remains until it leaves the nerve. Outside of the nerve it is much collapsed and folded, and still shows endarteritis, but both here and within the nerve the endarteritis is moderate and

* See some excellent pictures of this condition in a paper by Hertel (Arch. f. Ophth., vol. lii, pt. 2, p. 191).

the lumen not greatly narrowed. The *retinal veins* show very great changes indeed, of which an example is given in fig. 2. Considering the extreme tenuity of the walls of the normal retinal veins, it is at first sight difficult to believe that this is really a vein, but it can easily be proved to be so by following the vessels in the serial sections from the disc. It also refuses to take on Weigert's stain, and with this reagent gives the same appearance as the vessel to the left in fig. 1. It will be noticed that there is a very small blood-filled lumen, and that the layers next this lumen have a more granular aspect than the outer layers, take on eosin staining more freely, and have more rounded nuclei. These layers I take to represent proliferated endothelium. Outside we have a layer whose groundwork is more homogeneous and whose nuclei are fewer and more elongated. This I take to be the thickened connective tissue wall of the vein (there is, of course, no true media in the retinal veins). The wide space around the vessel is probably not an artefact, but the greatly dilated perivascular lymph space, and no doubt corresponds to the masses of exudation seen with the ophthalmoscope. Coagulated exudation will also be noticed in the inner layers of the surrounding retina. The membrana limitans interna is seen to pass over the vein without being broken through. These changes also are more marked towards the posterior pole of the eye, but are also present in the peripheral vessels. The peripheral veins are much engorged in places, those near the disc only very moderately so. As the veins pass on to the disc and through the lamina their lumina continue very narrow and their walls extremely thick, but as they do not unite to form the central vein for some distance back in the nerve, and as they are cut longitudinally at the optic nerve entrance, it is impossible to make any very definite statement as to how much obstruction would be caused, and as to whether any of them are obliterated. The surrounding connective tissue is much condensed. Coming now to the course of the vein *in the nerve*, it is at first divided into three or four branches, of which one only is very considerably thickened. These join together a little way behind the lamina, and the whole wall is now thicker than normal. Weigert's stain shows that there is much elastic tissue in the wall, and since the vein is collapsed and folded a false resemblance is given to a crenated membrane

such as occurs in the artery. That it is not a true elastica interna is shown by the high power, which resolves it into a large number of fine and coarse wavy fibres (fig. 3). Inside of this there is a tolerably thick layer of proliferated intima with scanty pale nuclei, and towards the lumen there is a pretty regular layer of endothelium. The lumen must be to a certain extent encroached upon, but it is still fairly large. It contains no blood. These conditions remain unchanged until the vein leaves the nerve, when it is much collapsed and folded, presenting merely a slit in the connective tissue, but always with an endothelium-clothed lumen. At no point is the vein completely obliterated, nor is any laminated or organised thrombus to be found within it.

Optic Nerve.—The optic nerve itself shows no atrophy. The sheaths are normal and the intervaginal space not dilated. There are a few concentric concretions between the arachnoid and dura and in the dura. There is no glaucomatous cupping.

This is in many respects an interesting case. It was followed closely practically from beginning to end, and undoubtedly presented the typical picture of thrombosis of the central vein with numerous hæmorrhages, and, what is of much greater importance to the diagnosis, greatly swollen and tortuous veins. There followed with unusual swiftness glaucoma, the eye suffered no more operative interference than a paracentesis, and was obtained for pathological examination just 21 days after the first dimness of vision and 8 days after the onset of glaucoma, so that it may be believed that no very extensive secondary changes had taken place. Yet no thrombus was found in the central vein, although it was examined to beyond its point of exit from the nerve. Outside of the nerve it was much collapsed, and there was thickening of the intima, but the lumen was not occluded. Inside the nerve there was a similar condition of the intima, but the lumen seemed easily sufficient for the transmission of the blood. The optic nerve entrance was unfortunately cut longitudinally, so that we cannot be quite certain as to what size the lumen was, as the vessel came through the lamina, but it may be said with certainty

that the thickening of the vein increased greatly at this point, and that the lumen was correspondingly reduced. Yet here also it seemed not to be completely obliterated. The retinal veins showed a thickening which, when we remember their extreme tenuity under normal conditions, can only be described as enormous.

The case also illustrates certain points with regard to the relation of glaucoma to these cases of hæmorrhagic retinitis, but I shall return to this subject later in discussing the subject from a more general stand-point. It is noteworthy in this case that the corneo-iritic angle was only very slightly blocked, and that the portion of the ligamentum pectinatum, against which the root of the iris did not rest, was quite free and spongy in texture, and seemed as if it ought to provide tolerably free drainage. This slight blocking is merely a stage towards a more extensive adhesion of the iris, and greater condensation of the ligamentum pectinatum, which is always to be found where glaucoma has long endured in these cases. It is evident that, however the glaucoma arises in the first place (and I shall discuss this later), it tends, the longer it endures, to perpetuate itself the more firmly by obliterative tissue changes at the corneo-iritic angle. In the cases to be mentioned immediately a more advanced condition of the same process will be described.

An interesting minor point is the finding of glistening yellow specks with the ophthalmoscope in one eye and of outgrowths of the membrane of Bruch with the microscope in the other, which makes the probability strong that such outgrowths are really the cause of these yellow specks.

Looking at the case as a whole then, the proof that there was any thrombosis to account for the clinical picture fails; the obstruction to the vein, which was evident with the ophthalmoscope, seems to have been entirely due to narrowing of the lumen in consequence of thickening of the vein wall (endo and periphlebitis), probably the result of a general angiosclerosis due to nephritis. Since, however, the

vessels as they passed into the eye were cut longitudinally, and not transversely, the possibility of a shrunken thrombus having been overlooked in this situation is not to be entirely set aside, for such a thrombus would explain better than a gradual process of obliteration the sudden loss of vision which characterised the clinical history. There is some proof that the site of obstruction was on the disc itself, inasmuch as the ophthalmoscope showed the veins greatly enlarged in the periphery, but hardly visible on the disc, while the microscope showed that the thickening of the vein walls was greatest on the disc, and that the veins central to the lamina were not engorged as they should have been if an obstruction had existed further back, but rather small, empty, and collapsed.

The following case presented a somewhat less typical history, but the pathological examination gave some results of importance. It was under the care of Mr. Simeon Snell, who has kindly furnished the clinical notes:—

Case II.

"Mr. D., æt. 53, consulted me on May 31st, 1902, and stated that in September, 1901, he was seized with giddiness, lost consciousness for 2 days, and on recovery was blind in both eyes. He recovered and was able to do things well until March, 1902. Then another attack came on, and since then he has been blind in the left eye. Vision in right is poor, 6/12. In the right there is haziness round disc (neuro-retinitis), but it is very little indeed compared to the left. In the left there is swelling of the disc with hæmorrhage. V. only l. p.

He has had 17 children, but only one is living, and that the youngest. He had syphilis 30 years ago. Not much headache or localising symptoms. Nose bleeds.

11.vi.02. A week ago he had seven fits. Right optic neuritis more intense. Left, a large number of fresh hæmorrhages like ecchymoses studded about the retina.

4.vii.02. Subsequently to last note he has had great pain with increased tension in left, and on this date the globe was removed."

The eye was preserved in spirit; it was shrunken and folded, but filled out again on immersion in 5 per cent. formalin.

Macroscopic Examination.—The corneo-iritic angle looks a little blocked. In the vitreous there is a coagulated exudate, but no fresh hæmorrhages. The retina is everywhere studded with hæmorrhages. The lens looks large, and nearly fills the interciliary space.

Microscopic Examination.—Serial sections were prepared of the globe as in the last case. The optic nerve was cut out along with the optic nerve entrance, and transverse serial sections were mounted from the retinal surface of the papilla through the lamina cribrosa and into the nerve.

Cornea Sclera, etc.—The cornea is normal. There is a moderate round-cell infiltration around the episcleral vessels and at the limbus, otherwise the sclera is normal.

Corneo-Iritic Angle.—As in the last case, the angle is much more extensively blocked on one side than on the other, the temporal. On the adherent side the occlusion is both more extensive—reaching nearly as far forward as the membrane of Descemet—and firmer. It is composed of fairly dense connective tissue, and the ligamentum pectinatum is itself much condensed, so that the spaces of Fontana are largely obliterated, and the canal of Schlemm, itself a mere slit, is shut off from any free communication with the anterior chamber. The ciliary processes are not pressed up against the root of the iris, but separated from it by a good interval. On the opposite side the amount of adhesion is nowhere so great, and, indeed, in some sections the angle looks almost free. The ligamentum pectinatum is also more spongy in texture, and the spaces of Fontana are patent, so that the canal of Schlemm, which is a wider channel than on the other side, seems to be open for drainage.

Iris, Ciliary Body, Choroid.—The iris stroma looks condensed and too cellular, but there are no definite inflammatory foci. The walls of the vessels are thickened, but there is no evidence of endothelial proliferation in this, as in the last case. A few small hæmorrhages are to be found in the substance of the iris near the corneo-iritic angle. There are no posterior synechiæ. The ciliary body is normal; the muscle is rather small. The choroidal vessels are collapsed, but not otherwise abnormal.

Retina.—The retina shows innumerable large and small hæmorrhages with corresponding distortion of its elements. They are mostly in the nerve-fibre and ganglion-cell layers, and in places bulge the membrana limitans interna sharply towards the vitreous, without, however, penetrating it at any place visible in the sections. They also penetrate the nuclear layers, but nowhere become subretinal. The retinal layers are on the whole fairly well preserved, though there is a good deal of scattering of the nuclear layers here and there by the hæmorrhages. There are many fibrinous and homogeneous coagula in the nerve-fibre layer and between the two nuclear layers, with a corresponding separation of the structures in these situations.

Retinal and Central Vessels.—In the larger *retinal arteries* the changes are very moderate and consist in endarteritis. In the smaller the affection seems to be chiefly of the middle coat, which has a clear homogeneous appearance with but little nuclear staining, *i.e.*, hyaline degeneration. On the disc the arteries are very considerably thickened, and in some cases nearly obliterated. The thickening seems to affect the media chiefly, and is in the form of a somewhat homogenous ground substance, in which, however, a faint fibrillation is visible, and in which there are comparatively few elongated nuclei. The lumen is much narrowed, but is lined by a single and even layer of endothelium. Farther back, just behind the lamina cribrosa and where the central artery is still undivided, we have the appearances shown in figs. 5 and 6. The media of the artery is seen not to be thickened, and to show the usual elongated muscle nuclei. Within this a normal elastica is visible, even without special staining, and within this again there is a very considerable thickening of the intima, which narrows the lumen in an eccentric manner. This consists of a somewhat granular but yet faintly fibrillar ground work, in which numerous small dark-staining nuclei are present. The lumen is lined with a single fairly regular layer of nuclei of the same size and staining reaction. It will be noticed that these changes are practically absent on one side, where the artery wall might pass as normal. The central artery contains only here and there a trace of blood. The above condition of endarteritis

persists in all the sections. Weigert's elastic tissue stain shows that there are some fine elastic fibres within the thickened intima.

With regard to the *retinal veins* the most important finding is shown in fig. 4. It occurs in a vein some distance out in the temporal periphery, and represents, I take it, a thrombus beginning to organise. It consists of a large rounded mass whose ground substance is partly homogeneous and partly granular, stains rather deeply with eosin, and shows here and there little groups of red blood corpuscles. There are also scattered groups of nuclei, a few only of which are polymorphonuclear leucocytes. The membrana limitans interna is bowed inwards at the spot, but is intact, and the internal nuclear layer of the retina is bowed outwards and thinned. There is copious hæmorrhage in the surrounding retina. For about two-thirds of its circumference the mass is separated off by a cleft which, however, is crossed by a few trabeculæ. In the remaining one-third there is the appearance of an invasion by young and cellular new-formed tissue. A little to the right there is a small thick-walled artery (out of focus in the figure). These appearances are only to be found in one vein; they are not present elsewhere in the retina. The other veins are much engorged, especially near the disc, and their walls are thickened, but the changes in them are on the whole very moderate. The veins on the papilla are moderately thickened, but slightly behind the base of the physiological cup they form a normal central vein, which continues without abnormality through the lamina cribrosa. Just behind this, however, we have the appearance shown in fig. 5. It will be seen that the circle of the vein is in a general way preserved and is of about the normal size. Its lumen is, however, traversed by a number of trabeculæ, so as to become divided into five loculi each containing blood. These trabeculæ are very thin, are continuous with the tissue of the vein wall, and are always clothed on both sides with a layer of somewhat flattened cells closely resembling endothelium. There is no undue cellular infiltration of the surrounding tissues. This appearance lasts for a few sections and then gives place to the state of things shown in fig. 6. The vein remains of about the same size, but in place of the trabeculæ crossing the lumen there is a little piece of organised

tissue free in the centre. It has a faintly fibrillar structure, and contains a few somewhat elongated nuclei, and in the centre there is again a tiny lumen containing blood corpuscles and lined with endothelium. The outer surface, that towards the main lumen of the vein, is also clothed with an even, single layer of endothelium. The space between this structure and the true vein wall contains a little blood, and the vein wall itself is normal and clothed with a single layer of endothelium. A little vein will be noticed just at this point entering the main vein from the surrounding trabeculæ. The vein now becomes normal and quite patent again. It accompanies the artery for a little way, but begins to part from it unusually soon, leaving only a few small normal venous twigs to accompany it. The vein now passes out towards the periphery of the nerve, and has just reached the pial sheath in the last sections, while the artery still remains in the centre. The vein beyond the point described above shows the ordinary feltwork of elastic fibres in its wall, but there is neither thickening of the wall nor endothelial proliferation.

Optic Nerve.—About the level of the lamina cribrosa, some of the optic nerve bundles show a closer grouping and deeper staining of their nuclei, and there are little wisps of convoluted nerve fibres. This is the condition described by Siegrist* as a pathological change, but proved by Elschnig† to be an artefact and due to the rough handling of removing the globe. The nerve is elsewhere slightly atrophic and unduly cellular. There are some concretions in its sheaths. The direction of the sections in this case makes it difficult to say whether or not there was a glaucomatous cup. If there was, it was at least neither a steep nor a deep one.

The clinical history in this case was not quite typical, inasmuch as both eyes were affected, which is a decidedly unusual circumstance in recorded cases. The left was, however, much more severely involved and showed very copious hæmorrhages, and the disease in this eye was in fact diagnosed by Mr. Snell intra vitam as a thrombosis of the

* Siegrist, Arch. f. Aug., vol. xliv, Ergänzungsheft, p. 178.

† Elschnig, Klin. f. Aug., vol. xl, 1902, p. 81.

central vein. It is not improbable that the fits, giddiness, and loss of consciousness described were due to thrombosis in the cerebral vessels, and it is to be noted that after one of these attacks many fresh hæmorrhages were found in the retina. This eye was not interfered with by iridectomy or sclerotomy.

As in Case I, there were no hæmorrhages in the vitreous, though it is possible that the coagulated exudate mentioned may have represented a previous hæmorrhage. The condition of the corneo-iritic angle was much the same in the present case as in the former, but the changes were rather more advanced. It is probable that this corresponded with a longer duration of glaucoma.

That the peculiar appearance shown in fig. 4 represents an organising thrombus, there can, I think, be no doubt. It is of rounded form, it is surrounded by fine connective tissue, it has a small artery in its neighbourhood, and the inner nuclear layer is bowed out at the position which it occupies, just in the manner usual where a large vessel runs in the retina. All these things point to the fact of its being a much distended vein. That the cause of this distension was a thrombus, is shown by the presence of red blood corpuscles among the more homogeneous groundwork. That this thrombus was organising, is shown by the groups of nuclei within its substance and by the invasion from one side of new-formed connective tissue. No other explanation seems feasible. It is too large, rounded, and well-defined to be one of those coagula which are met with in albuminuric and other hæmorrhagic forms of retinitis, usually between the two nuclear layers, but sometimes in the inner layers of the retina. Such coagula were present in this case, but they always showed a squared-off form from lying in the rectangular spaces between the fibres of Müller, nor did they ever show any signs of organisation. It cannot be merely an organising hæmorrhage, for, on the one hand, its boundaries are too definite, and on the other it is surrounded by abundant hæmorrhage, which is evidently not organising.

We must, I think, undoubtedly regard it as a thrombus in a vein within which organisation has begun, but not progressed very far.

With regard to the very unusual appearances shown in figs. 5 and 6, I think the same explanation must be given—that they represent a thrombus, but in this case fully organised and canalised. Indeed, the two appearances give mutual support to this explanation; for if the body in the peripheral retinal vessel is indeed a thrombus commencing to organise, there is nothing strange in finding a more advanced stage of the same process in the central vein. Here, again, it is difficult to think of any other feasible explanation. It is evident that we have not here to do with a division of the vein into branches, for it can be plainly seen in the photograph that these trabeculæ (enclosing spaces of such different sizes) are all included within the normal circle of the vein. Further, the appearance is practically the same through several sections, while only a short distance in front of and behind the place shown in figs. 5 and 6, the lumen of the vein is quite normal and single. The little mass in the centre of the lumen in fig. 6 is to be regarded as the transverse section of a pointed process in which the thrombus ended. As a minor confirmatory point, it may be noted that the appearance ceases where a little tributary joins the vein, and it is, of course, well known that thrombi in veins usually extend to the nearest collateral. In Case I there was a true division of the vein a little way behind the lamina, but at no place in the series were the appearances at all like those in the present case. Judging by the different degrees of organisation in the two positions, it is probable that thrombosis occurred first in the central vein and at a later date in the retinal vein. It may be that the central vein was affected at the first loss of vision, and that the retinal vein subsequently became thrombosed about the time when the "large number of fresh hæmorrhages" was noted.

It may be asked, if there was complete organisation of a thrombus in this manner with restoration of the circulation,

why was there no restoration of vision? It must be remembered, however, that the retinal elements would be largely destroyed by the blood already poured out, and would be incapable of recovery. Further, that when glaucoma had occurred (a condition which has been shown to tend to be self-perpetuating), the restoration of the circulation through the central vein would make no difference to the vision, since the seeing elements would still be destroyed by the continued high tension. Evidently when actual adhesions had occurred at the corneo-iritic angle the restoration of the retinal circulation could make no difference to them.

The endarteritis in this case may have been merely part of a general angiosclerosis, when it would, no doubt, to some extent favour the occurrence of the thrombosis in the vein by narrowing the arterial lumen, and so slowing the blood stream, and perhaps interfering with the regulating mechanism. It may also have been wholly or in part secondary to the damming back of the blood caused by the venous obstruction, since obstruction of a vein is known to produce changes in the corresponding artery.

It is noteworthy that in this eye the vein pursued a rather unusual course; it left the artery quite a short distance behind the lamina and curving quickly outwards soon passed out of the nerve. It is possible that this sudden curvature of the vein was the factor which determined the laying down of the thrombus in the position which it occupied, for such a curvature would constitute some hindrance to the return flow of blood, a hindrance which might have been sufficient to cause a thrombus to be deposited on its distal side rather than elsewhere, provided that the general conditions were favourable to the process of thrombosis, and such conditions seem to have obtained in this patient to judge by his history of cerebral attacks. This may also have been the reason why the left eye was attacked rather than the right.

Case III is also chiefly of interest from the pathological aspect. The clinical history from our present point of view

was somewhat defective, inasmuch as the eye was blind and glaucomatous, when first seen, and the media were too opaque to permit of an examination of the fundus. The condition of hæmorrhagic retinitis was, therefore, not diagnosed intra vitam.

Case III.

Martha C., æt. 62, was admitted to the R.L.O.H. on 28.ix.03, under Mr. Tay. The left eye was blind, but how long it had been so was doubtful. It had been painful for 9 days.

V. R. 6/18 $\bar{c}$ + 1 = 6/9. Tn.

V. L. Hand movements. No. K. P. Fair A. C. Iritis. No view of fundus. T + 2.

The urine contained a trace of albumen. No sugar, sp. gr. 1010.

On 1.x.03 a paracentesis of the anterior chamber was done by Mr. Collins, and again on 5.x.03. On the first of these occasions there was hæmorrhage from the iris.

7.x.03.—Cornea hazy. A. C. good. Iris dull, 1/3 dilated. Posterior synechiæ T + 2. An iridectomy was therefore performed on 12.x.03, and gave at the time relief from tension and pain.

5.xii.03.—Readmitted. Left painful. Scar bulging. Cornea hazy. K. P. Hyphæma. A. C. shallow above. Outer angles of coloboma drawn up. Lens opaque and swelling. T + 2. V. L. shadows.

The heart was irregular, and there was occasional loud systolic bruit at the apex ? mitral regurgitation.

16.xii.03.—Excision. The eye was hardened in formalin and bisected sagittally.

Macroscopic Examination.—Scar cystoid; hyphæma; lens absent; retina *in situ* covered with hæmorrhages; no hæmorrhage in vitreous; choroid *in situ.*

Microscopic Examination.—Sections were prepared as in the previous cases.

Cornea.—Œdematous spaces are present among the deepest layers of the corneal epithelium. The iridectomy wound is some distance from the corneo-iritic angle. Its two lips are covered with new-formed fibrous tissue, and are not in apposition, the lower lip being in front of the upper. There is much pigment in the

wound which is covered by conjunctiva. To the upper lip of the wound the iris stump is adherent, while the iris from the opposite side has been dragged over and has become adherent to the lower lip. It thus happens that what remains of the anterior chamber is entirely shut off from the wound, which opens direct into the vitreous chamber. The lens had escaped through the wound. For a considerable distance from the edge of the wound there is a layer of new-formed tissue between Bowman's membrane and the epithelium, and in a similar area the superficial layers of the cornea have become cicatricial and vascular, and have lost their even arrangement in layers. Otherwise the corneal stroma is normal.

Corneo-Iritic Angle, Iris, etc.—The iris is adherent to the whole of the ligamentum pectinatum, and for some distance to the back of the cornea. The ligamentum is much condensed, and the space of Fontana are obliterated. There is blood in the anterior chamber. The iridectomy stump is highly atrophic and its vessels are much thickened. The foremost ciliary process is displaced forwards and adherent to it. The iris on the opposite side is somewhat condensed, but shows no vascular change. The ciliary body is much atrophied, especially on the side of the iridectomy. The choroidal vessels are mostly empty, but the choroid seems normal.

Retina.—In addition to the distortion caused by the copious hæmorrhages this case showed definite inflammatory lesions in a few places. The retina is adherent at these spots to the choroid, the pigment epithelium having disappeared, the retina has a more fibrous appearance than normal, and the nuclear layers are greatly distorted. Apart from these patches the nuclear layers are well preserved on the whole. The nerve-fibre and ganglion-cell layers are highly atrophic, and in places œdematous. The hæmorrhages are extensive and are mostly in the inner layers of the retina, but pass through the nuclear layers in places and cause large subretinal extravasations. There is also a little blood in the vitreous, but its connection with any of the retinal vessels cannot be traced in the sections. There are no coagula between the nuclear layers. Near the ora serrata the retina is much atrophied, and there is some in-wandering of pigment from the pigment epithelium.

Retinal and Central Vessels. — The *retinal arteries* show but little change. Some of the smaller vessels in the periphery are obliterated, or have their lumen greatly narrowed by a hyaline-looking thickening of their walls, but it is doubtful whether these are arteries or veins. The central artery behind the lamina shows a very considerable endarteritis. It is of the type already described, except that in places the proliferated cells of the intima which compose it have a clear blown-out appearance, not present in the former cases. A specimen stained with Weigert's elastic stain is shown in fig. 11, which represents well the thick (in this case unusually thick) crenated membrane. Within this can be seen a feltwork of curled elastic fibres, fine and coarse, among which there are a few nuclei. The space which separates these fibres from the crenated membrane corresponds to a group of the blown-out looking cells which have just been mentioned, though part of the appearance is perhaps caused by a little obliquity of the section. Where the vein wall is thickened (*vide infra*) the arterial lumen becomes very small.

The *retinal veins* are not greatly engorged. They show considerable thickening, somewhat similar to that shown in fig. 2, but less extensive. There is also less appearance of endothelial proliferation; the lumen is lined by a single layer of endothelium, then comes a clear staining, thick layer with rather scanty but well-stained elongated or oval nuclei. The ground-substance is not hyaline, but finely fibrillated. This layer is sometimes separated from the surrounding tissues by a cleft, but the wall looks shrunken in these places, and it is probably an artefact and not a dilatation of the perivascular lympth spaces as in fig. 2. The central vein is formed by the junction of its branches just in front of the lamina, and at the bottom of the glaucomatous cup. Its wall is at first condensed, but there is no endothelial proliferation or narrowing of the lumen. The connective tissue surrounding the central vessels is here also much condensed. A little further back—toward the posterior part of the lamina cribrosa—the appearance shown in fig. 7 is seen. The surrounding connective tissue is still very dense, and the artery has a good free lumen containing formed blood corpuscles. The vein lumen is relatively small, smaller than that of the artery, but it has still a fair diameter, and there is

no sign of endothelial proliferation. Within the lumen and lying to one side of it there is a rounded homogeneous coagulum, around whose edge there are a number of polymorpho-nuclear leucocytes and a few red corpuscles, while the central area is clear. The remaining part of the lumen contains no blood corpuscles. Tracing the vein backwards, its lumen now becomes narrower, and the coagulum becomes closely plastered up against one wall and more cellular. The lumen now seems to become encroached upon by the neighbouring fibrous tissue, so that it is cut in two, a little lumen being left at one side and a larger at the other. The larger of the two contains a little coagulum. Next we have the appearance shown in fig. 8. The vein is almost entirely replaced by a little knot of loose new-formed fibrous tissue, more cellular than the surrounding connective tissue. There is still, however, some trace of a lumen at each end. The vessel now disappears almost entirely, and its position is only marked by a slightly more cellular area in the connective tissue, without any trace of a lumen. Indeed its proper position could hardly be told from the mere examination of this section, but can easily be located by taking a bearing of the unobliterated and of the obliterated vein from structures which pass uninterruptedly through the series. At this point a moderate-sized collateral appears from the trabeculæ of the optic nerve on the side of the artery *opposite* to the obliterated central vein, and this shortly turns backwards and accompanies the artery by which it is separated from the position of the true central vein (fig. 9). It contains some coagulum similar to that in the central vein before its obliteration, and this coagulum also is shrunken and infiltrated with leucocytes. While this false central vein is still accompanying the artery a small twig enters the tissue in the position of the true vein (fig. 9), and presently the lumen is restored. It is, however, very small, and the vein is extremely thick-walled. Presently the vein which came from the trabeculæ on the opposite side joins with this small lumen, which becomes, therefore, larger, but still not so large as normal (fig. 10). It gradually gets somewhat larger by the accession of fresh collaterals. To the end of the sections (which do not reach the point of exit of the vessels from the nerve) the vein wall

remains enormously thickened. The thickening shows fine wavy fibres in its substance and a few oval nuclei. The vein lumen is clothed with endothelium, and contains no coagulum, but normal blood corpuscles. With Weigert's elastic tissue stain there are only a few very fine curly fibres in the thickening. The main mass of the elastic fibres are outside, where they form a false crenated membrane in the manner already described. Briefly stated, therefore, the changes in the vein amount to obliteration for a space with re-establishment of the lumen where collaterals join it.

Optic Nerve.—There is a deep glaucomatous cup with very steep edges. It reaches almost to the scleral ring in one direction, leaving only the thinnest possible layer of tissue, from which all trace of emerging nerve fibres seems to have disappeared. There is some hæmorrhage within the cup. The lamina itself forms a meshwork from which practically all the nerve fibres have disappeared. Further back in the nerve the atrophy is very extreme. The nerve is extremely shrunken, the trabeculæ are thickened, and it looks unduly cellular. Two nearly opposite sectors, however, are especially marked out by the extreme degree of the atrophy which they present. No nerve fibres at all are to be seen within the trabeculæ. The two sectors together take up about one-third of the nerve. They correspond perhaps to the places where the nerve fibres were most severely nipped in crossing over the edge of the cup, but I could not with certainty trace this relationship, because the arrangement into sectors becomes less definite near the lamina.

The pathological changes in the anterior half of this globe are not of much importance to the present inquiry, because the eye had been interfered with by iridectomy 2 months before it came to excision, and, therefore, it is impossible to say with regard to some of the changes whether they were due to the disease itself or secondary to the operation. It may simply be stated that the blocking of the corneo-iritic angle was much more complete than in Cases I and II.

In this case there was hæmorrhage into the vitreous,

but, of course, in an eye which had been subjected to an iridectomy, and which was not excised for nearly 3 months after the onset of glaucoma, it is impossible to say when the vitreous hæmorrhage occurred and what relation it may have had to the causation of the glaucoma. The deep cupping of the disc in this case was a sign of the long continuance of the glaucoma, and so probably was the extreme atrophy of the nerve.

With regard to the retinal changes it may be noted that whereas in Cases I and II there were no signs of retinal inflammation, but only of that distortion of the retinal elements by the out-poured blood which usually goes under the name of hæmorrhagic "retinitis"; in the present instance there were signs of true inflammation in the patches of fibrosis mentioned above.

The chief interest of the case, however, lies in the condition of the central vein. Following it backwards we have first a normal lumen, then an area of complete obliteration, then, after it has been joined by collaterals, a space in which the lumen reappears, but is greatly narrowed by an enormous thickening of the vein wall. The coagulum I believe to be merely a *post-mortem* clot, or, at least, to have been deposited from completely stagnant blood; it shows neither the lamination of a thrombus deposited from flowing blood nor the organisation which one would expect in a thrombus of some duration. The slight infiltration of its edge with leucocytes might quite well, I think, have occurred in the time between the molar and the molecular death of the tissues. Further, similar appearances were present in some of the ciliary arteries. I have already spoken of a similar appearance, described and figured by Michel as a "thrombosis" of the central vein, in one of his cases. The appearance which succeeds this in following the vein backwards is, however, evidently quite a different thing. The vein becomes entirely replaced by a little knot of connective tissue not very different from the surrounding connective tissues, but easily enough distinguished by its

greater cellularity, and this little knot can be readily proved to be in the exact position of the vein by its relation to surrounding structures, which run unaltered through the series. Besides, there is for a space no other vein accompanying the artery which could be the central vein proper (fig. 8). There can, I think, be no doubt that this is an organised thrombus which has failed to canalise as in the last case, but has gone on to complete obliteration. That it is not merely an obliteration by endothelial proliferation is shown by a high power examination of its structure, which shows it to be made up not of thick-walled vein, but of young connective tissue. Its extreme shrunkenness, indeed, is almost sufficient of itself to prove the fact. It was not possible in this case definitely to state that the collaterals in the trabeculæ of the nerve corresponding to the obliterated portion of vein were enlarged, but this is hardly to be wondered at, for these collaterals are many and the blood would be distributed among them all, so that each one would be but little more engorged than normal. The extensive retinal hæmorrhages show that the collaterals were not efficient for the carrying off of the dammed back blood.

With regard to the great thickening of the vein wall central to the obliterated portion, its significance is not quite certain. It may be that it was present before and helped in the determination of the thrombosis, or it may be that the meagre blood stream and collapsed condition of the vessel after the occurrence of the obstruction in some way helped to cause the thickening of the wall. At any rate, it is remarkable that the vein should be so very thick central to the obstruction and so relatively thin on the bulbar side. The extreme atrophy of the optic nerve is to be attributed to the long duration of glaucoma and the depth of the cupping.

Case IV is very similar to the last and may be more briefly reported. Mr. Flemming, under whose care the patient was, has kindly supplied the clinical notes.

Case IV.

"Mr. B., æt. 59, was first seen 11.xi.03. The right eye had been failing gradually. V = hand movements. O.E. Much retinal œdema, and numerous hæmorrhages in the nerve-fibre layer for the most part. Nasal border of optic disc obscured by the swollen retina. Veins very engorged and tortuous. Arteries are hidden by the swollen retina, and are only to be made out here and there.

Urine sp. g. 1,012. Trace of albumen; no sugar. Arteries rigid, but no organic cardiac disease.

19.xii.03. Eye painful; tension +2; cornea hazy; pupil small; no p.l.

23.xii.03. T + 3. Eye excised; much bleeding in attempting to divide the nerve long. Much bleeding at two subsequent dressings, requiring the orbit to be plugged." A portion of the very long nerve which Mr. Flemming had secured was unfortunately lost, so that the sections do not extend beyond the point of entrance of the vessels. The eye was preserved in formalin, and bisected horizontally.

Macroscopic Examination.—The corneo-iritic angle looked only a little blocked. There was no blood in the anterior chamber nor in the vitreous. A large mass of exudation hid the situation of the disc, and from within it the obviously enlarged and tortuous veins appeared. It caused a swelling of about 1 mm. Large hæmorrhages were present in every part of the retina, and a few white plaques.

Microscopic Examination. Cornea, Sclera, etc.—A few vesicles in the corneal epithelium. Stroma normal. Limbus and episcleral vessels moderately infiltrated. Sclera normal.

Corneo-Iritic Angle.—This is blocked by adhesion of the root of the iris to the ligamentum pectinatum, usually for about half its extent, though in places the adhesion reaches as far as the membrane of Descemet. Where the adhesion is most extensive there is a certain amount of condensation of the ligamentum, with obliteration of the spaces of Fontana, but on the whole this is moderate, and in some sections but little marked. There are a few small blood extravasations in the root of the iris, and in the spaces of Fontana.

Iris, Ciliary Body, and Choroid.—The iris stroma is normal, and the vessels only moderately thick walled. The ciliary body is normal. The choroidal vessels are mostly empty and collapsed, so that the choroid looks thin. There are a few hyaline outgrowths of the membrane of Bruch.

Retina.—The retina contains some very large hæmorrhages near the disc, and in this situation the retinal layers are much distorted and their nuclei widely scattered. The remainder of the retina is infiltrated in every part with blood, but none of the hæmorrhages are very large, and the nuclear layers are tolerably distinctly preserved. As is usual, the hæmorrhage is most abundant in the nerve-fibre and ganglion-cell layers, but it has permeated all the layers in places, and there are both pre-retinal and sub-retinal hæmorrhages. A few homogeneous coagula are present between the nuclear layers. There is a moderate amount of vacuolation near the ora serrata, and there are some nuclei among the rods and cones.

Retinal and Central Vessels.—Some of the smaller vessels in the periphery show a true hyaline change. They have a glistening, homogeneous aspect, involving the whole wall, and show no nuclear staining. Whether these are arteries or veins is uncertain. The changes sometimes amount to obliteration. The *retinal veins* are moderately engorged. They show a considerable thickening of their walls, which is fibrillar, and contains well-stained spindle-shaped nuclei. The endothelium seems not to be proliferated, and the thickening is apparently confined to the connective tissue wall. It does not look hyaline. The central vein is formed just in front of the lamina, and here it is much distended with homogeneous coagulum and well-formed red blood corpuscles. A few sections further back, but still within the lamina cribrosa, the vein suddenly disappears, and there is no vein at all accompanying the artery, unless a little slit in the connective tissue at one side represents it (fig. 12). This slit, however, is not lined by any regular endothelium, and its wall consists of connective tissue entirely similar to the connective tissue around, so that it is probably merely an accidental cleft in the tissues, perhaps caused in the preparing of the sections. The surrounding connective tissues show no undue cellular infiltration. There are many much

engorged collateral branches in the surrounding nerve trabeculæ in the area within which the vein has disappeared. The exact manner of the disappearance of the vein can unfortunately not be demonstrated in this case as it was in the last, for only every fourth section in the series was mounted. In one section the vein was present and distended, in the next it was absent, as is shown in fig. 12. In the section following, two very small veins appear in the position formerly occupied by the main vein, and these presently join together (fig. 13) to form a larger, but still very small, central vein. These two veins contain well-formed red blood corpuscles. Following the vein backwards, it is found to receive many small and large collaterals from the surrounding trabeculæ, by the accession of which it gradually resumes its normal size and remains normal in size to the end of the series (fig. 14).

The retinal arteries are much thickened, and in places nearly obliterated. The thickening is cellular, and suggests endothelial proliferation. In front of, and within the lamina, the artery is much distended by homogeneous coagulum with leucocytes in the periphery and red blood corpuscles in the centre. This coagulum has sometimes shrunk and pulled away the intima of the vessel, evidently a *post-mortem* appearance (fig. 13). There is at this point no endarteritis, but in following the artery back thickening of the intima gradually appears, until finally, where the vein reattains its normal size, the arterial lumen has become smaller than the venous. Next, the formed red corpuscles within the lumen begin to be replaced by homogeneous coagulum, in which there are a few leucocytes, and a little farther back these leucocytes are replaced by elongated cells, the groundwork being still homogeneous. The lumen now becomes filled with an organised mass, the substance of which is composed of coiled-up wisps of fine fibres, among which spindle-shaped nuclei are visible (fig. 14). There are no capillary vessels within it. The mass is separated from the vessel wall by a cleft which is complete all round, and not bridged in any of the sections (every fourth), and within this cleft there are a few red blood corpuscles. There is much endarteritis at this point. This appearance lasts for a few sections, and is then replaced by more homogeneous coagulum with elongated nuclei, and finally by normal red blood corpuscles. The endarteritis becomes less from this point to the end of the series.

Optic Nerve.—There is no glaucomatous cupping. The nerve itself is moderately atrophic and unduly cellular. There are some concrements in the arachnoid sheath.

This case shows many points of resemblance to the last. Clinically it differed, inasmuch as the diagnosis of thrombosis of the central vein was made intra vitam, and the hæmorrhagic retinitis was therefore definitely known to have preceded the glaucoma. The blocking of the corneo-iritic angle was moderate, both in extent and in degree, and the spaces of Fontana seemed to be left fairly free for drainage. The retinal changes were entirely those of distortion from extravasated blood ; there were no inflammatory infiltrates. The retinal vessel changes were those of proliferation and degeneration ; there were no thromboses within the lamina cribrosa.

The disappearance of a certain length of the central vein, without leaving a trace, is certainly a noteworthy fact. We have presumably the same changes as in Case III, but they have gone a step farther, and the new-formed connective tissue has totally cicatrised and become indistinguishable from the surrounding tissues. Were it not for the findings in the last case, by which we can trace the process of cicatrisation, we might almost be tempted to believe that we had to do here with a congenital peculiarity—that a portion of the vein was congenitally absent, and that its place was taken by enlarged collaterals among the nerve. That, however, is a condition which, so far as I know, has never been described. It is to be remembered that we are not dealing with an early division of the vein, for, both in front of and behind the obliterated portion, it has a normal lumen. Then again, we have seen, in the last case, the vein *almost* disappear, its position being only marked by a little cellular infiltration. Further, we have to remember that obliteration of the vein accounts for the clinical symptoms of venous obstruction, which are not otherwise accounted for by anything in the pathological examination. So that

there seems to be sufficient proof that we really have here a pathological lesion which has affected a smaller length of the vessel than in Case III, and whose stages, therefore, cannot be so exactly followed.

With regard to the little cellular plug in the artery, there can, I think, be little doubt that it is an organised thrombus, and that the thrombosis in the artery was secondary to the interference with the blood flow, caused by the occlusion of the vein. In the first place, the changes in it are not so advanced as those which have obliterated the vein, and, therefore, it is presumably younger. Then again, if the arterial plugging were the primary lesion, the venous obstruction and hæmorrhages seen with the ophthalmoscope would be totally inexplicable. The symptoms were at no time those of thrombosis of the central artery, a lesion which has been several times proved to give the picture of "embolism" of the central artery, and which is, in fact, probably at the root of most, if not all, of those cases of so-called "embolism." That it is an organised plug, foreign to the vessel, and not an endarteritis, which has gone on to complete obliteration, is evident at a glance, from the histological difference between the mass in question and the endarteritis, which is also present. Besides, there is quite a definite cleft between the two containing blood. It is certainly somewhat difficult to account for the fact that this cleft is complete all round, and that nowhere in the sections is it bridged over by connective tissue, for it is evident that the process of organisation, which is essentially a reaction of the surrounding tissues, cannot but result in the intimate union of the plug in the lumen and of the tissues in the vein wall. It may be that there *is* a connection with the vessel wall somewhere, but not in the present series, which includes only every 4th section; or again, this may be a a form of canalisation in which the clot itself is not channelled (as in Case II), but in which the blood has found its way by the side of the thrombus, and, aided by the shrinkage of the new-formed connective tissue, has finally

succeeded in making a cleft between it and the vessel wall right round. It might be argued that the presence of a complete cleft proves that the plug is really an embolus, *i.e.*, that a fibrous mass formed elsewhere in the vascular system had become detached and swept into its present position, and that the reaction of the surrounding tissues had not yet commenced. But, if so, whence did it come in the present instance, and how can it be fitted into the history of the case? It would be necessary to regard its presence as a mere coincidence, which seems a very unlikely supposition.

The most probable view of the sequence of events here, then, seems to be that there first occurred a thrombosis of the central vein at its narrowest part, where it passes through the lamina. The general arteriosclerosis and the nephritis present in the case very probably bore a part in causing it. This thrombus became organised in the ordinary way, but failed to canalise, and sufficient time elapsed for the new-formed connective tissue to totally cicatrise and disappear. In the meantime (at what stage exactly must be uncertain), the hindrance to the circulation caused by this occlusion reacted on the blood flow in the artery, and, at a point where the lumen was already narrow from endarteritis, a thrombus occurred, and in its turn also organised. It is not likely that any change would be brought about in the clinical symptoms by this occurrence, for the retina would already be the seat of an intense hæmorrhagic retinitis from the venous plugging, and the plugging of the artery, in addition, would make but little difference. The next stage may have been, as argued above, an imperfect channelling between the thrombus and the artery wall, which resulted in some degree of restoration of the arterial current, and caused the separation of the thrombus from the wall by a narrow cleft.

Four cases have now been given in which the appearances known clinically as "thrombosis of the central vein" were either seen ophthalmoscopically intra vitam, or were found macroscopically when the eyes were bisected after hardening

Of these, three showed evidence that there had really been a thrombus to account for the symptoms, and the successive stages in the processes of thrombosis and organisation may be roughly indicated by figs. 4, 5, 8, and 12. It has been already pointed out that some uncertainty remains with regard to Case I, because the optic nerve entrance was cut longitudinally, for it will be readily understood how little could have been said with certainty of the changes shown in figs. 7 to 11 (for instance) if the sections had passed longitudinally to the nerve entrance in the usual manner instead of transversely. The number of my cases is still too small, but they lend support to the belief that if some of the other cases in the literature had been treated in the same manner, more definite results might in some instances have been obtained, and the disease in question given a firmer and more consistent pathological basis. One may hope that more records of pathological examinations of these cases may be published.

It remains now to discuss certain problems raised by cases of this sort, and to see how far they are illustrated by the cases described. The chief of these problems may be briefly stated as follows: (1) What general and local conditions favour the occurrence of thrombosis of the central vein? (2) Why does glaucoma so commonly follow in these cases? (3) What is the exact nature of the changes found in the central and retinal vessels, and how much of them is primary and how much secondary to the onset of thrombosis and glaucoma?

Chief among the causes of thrombosis of the central vein must undoubtedly be counted angiosclerosis, including in this term all those conditions which tend to the thickening of vessel walls and the narrowing of their lumina, and including affections both of arteries and of veins. An examination of the literature shows that out of 26 cases arteriosclerosis of the systemic vessels was present in 11, absent in 8, and not mentioned in 7. Schoenewald* found

* Schoenewald, quoted in Nagel's Jahresbericht, 1900, p. 620.

arteriosclerosis present in 7 out of 18 cases. In 9 cases personally observed it was present in 4 and absent in 5. These figures do not give so large a proportion with arteriosclerosis as might have been expected from some of the descriptions of the disease, in which rigidity of the radial and temporal arteries is stated to be nearly always present. It may be noticed in passing, that while arteriosclerosis of the peripheral vessels is a valuable guide pointing to the probability of arteriosclerosis being present in the vessels of the eye, its absence cannot be taken to mean absence of vessel change within the eye-ball. In Case I, for instance, in which the changes in the retinal vessels reached the very high degree shown in fig. 2, there was no evidence of arteriosclerosis in the peripheral vessels, and I have seen this also in another case, which I had the opportunity of examining microscopically. The same thing is well-known to obtain in the case of the cerebral vessels, which are sometimes highly sclerosed, although no evidence of general arteriosclerosis is furnished by the peripheral arteries. There may even be extensive microscopic changes in the retinal arteries without ophthalmoscopic evidence as Hertel* has recently shown. It is, however, true that in nearly all the cases of thrombosis of the central vein which have come to microscopic examination the vessels have been found extensively diseased. It was certainly so in all four of my own cases, and in two others of which I made a partial examination.

It follows that if angiosclerosis be a cause of thrombosis, the conditions which favour the occurrence of angiosclerosis must also be included among the causes of thrombosis. Of these the chief are old age, heavy strains, nephritis, and perhaps syphilis.

The influence of old age is best represented in tabular form, as follows:—

* Hertel, Arch. f. Ophth., vol. lii, pt. 2, p. 191.

Age.	Cases from literature.	Personal observations.
1—20	1	—
20—40	5	2
40—60	8	6
60—80	10	1
80—90	1	—

The figures of Ammann* may also be quoted, who found among 60,000 patients in Haab's clinique 20 cases of thrombosis of the main venous stem, of whom 15 were between the ages of 50 and 80, and 2 of the others, æt. 47 and 29 respectively, had heart disease and arteriosclerosis. There figures are sufficient to show how the disease increases with increasing age, a fact which is of common experience. Nearly all the cases occurring under 40 are of an unusual type, and in some of them the diagnosis is doubtful.

Ammann has especially called attention to the frequency with which those suffering from thrombosis of the central vein are persons accustomed to much toil, and especially to much stooping. He found that 13 out of his 20 cases were either peasants or persons who did gardening for pleasure, while 2 others were smiths. We have here perhaps both a remote and an immediate cause of the affection, since constantly repeatedly strains would tend to cause angiosclerosis, while the venous congestion caused by some especially violent strain might be the cause of the actual thrombosis. It is because of their greater liability to physical strains, Ammann believes that more cases occur among men than among women. My own experience has given 4 cases in males and 5 in females, but this is probably a coincidence, since it is undoubted that men considerably predominate in the reported cases (16 to 8).

With regard to the influence of nephritis, it will be found that this is less prominent than might have been expected. Out of 26 recorded cases it is only mentioned

* Ammann, Deutschmann's Beiträge, Heft. xxxviii, 1899, Heft. xxxiii, p. 1.

5 times, in 5 it is not noted whether it was present or absent, and in 16 it was not present. Among my own cases it was present 4 times, absent twice, and not noted twice, so that it was present in a much larger proportion than in the cases in the literature. In any case it is to be regarded not as a direct, but as an indirect cause, it will act presumably merely by helping in the causation of angiosclerosis. Syphilis is usually credited with having a considerable influence in the etiology of angiosclerosis, *vide* the frequent history which one obtains of it in cases of aneurism. Yet it is very seldom mentioned in the reports of cases of thrombosis of the central vein, and I have only met with one case personally in which a clear history of it was obtained.

Angiosclerosis, then, may be given the first place in causing thrombosis of the central vein. Yet all cases do not seem to be so explained, and among other causes valvular heart disease must be mentioned. I may very briefly quote the following case in illustration.

Margaret M, æt. 25, had noticed a dimness in the sight of the left eye a fortnight before she presented herself for examination. She had suffered since early childhood from "heart disease," of which the origin was obscure, since there was no history of acute rheumatism or of chorea. She had long been liable to be laid up at times with attacks of cardiac insufficiency, and this had happened 3 months before she was first seen. Loss of vision was sudden, without any prodromal phosphenes, etc., and in the form of a uniform grey veil before the eye. She was at the time in her usual impaired health—not confined to bed.

The patient was very breathless and cyanosed, and had some œdema of the ankles. The heart's action was very "tumultuous" and irregular; there was pre-systolic thrill, and a rough murmur preceding and running into the first sound of the heart. The diagnosis with regard to the cardiac condition was "mitral stenosis with cardiac insufficiency."

V.R., 6/6 and Ji. O.E. normal.

V.L. Shadows. O.E. The fundus strewn in every direction

with large hæmorrhages, striate, round and irregular, with here and there among them, yellow patches. The disc was encroached on by hæmorrhages from all sides. The arteries were hardly visible, the veins much swollen, very dark and tortuous; in fact the typical picture of thrombosis of the central vein.

There seemed to be no other cause for the occurrence of a thrombosis in this instance than the interference with the venous circulation brought about by the mitral stenosis. The patient was too young to make it probable that she had angiosclerosis, even in the presence of valvular heart disease, and there was certainly no proof of it in the peripheral vessels. A somewhat similar case of Juler's has been already mentioned. Valvular disease has also been present in some of the other cases in the literature (*vide* Michel's Case I, Türck's, Meyerhof's), but either associated with evident arteriosclerosis, or occurring at an age when arteriosclerosis might be expected to be present. Schoenewald gives 3 cases out of his 18 as suffering from heart disease.

It might be expected that weakening illnesses might occasionally be followed by a thrombosis of a marantic nature, but it seems that this is seldom the case. The patients are usually apparently in their ordinary health. I have, however, in 3 cases obtained a history of influenza, a disease which is known sometimes to cause thrombosis in the cerebral vessels. In two of them dimness of vision occurred during convalescence, and in one about a month after an attack. I should not, however, be inclined to lay too much stress on the influenza as a causative factor, for the patients were not in any of the instances reduced to any very profound state of debility. To a similar category may be referred the case of Würdemann, in which thrombosis of the central vein followed a fortnight after an attack of mumps in a boy of 8. Also possibly marantic was Case II of Michel's mentioned in the table, in which a thrombus was found in the central vein of a patient who died of leukæmia, and a case of Ballaban's* (not proved pathologically) in a

* Ballaban, Arch. f. Augenh., vol. xli, p. 280, 1900.

girl suffering chlorosis. Goh's case may also be mentioned here, in which a hæmorrhagic retinitis appeared 3 days before death from septicæmia, and in which a thrombus was found in the right central vein. It is a noteworthy point (first mentioned by Michel) that in not a few cases dimness of vision has been first noticed on awakening in the morning. This was the history in the cases of Bankwitz and Wagenmann (Case I), and I have myself obtained it in 3 out of 9 cases. It probably merely signifies that, given conditions favourable to the occurrence of thrombosis (angiosclerosis, etc.), the lowered blood pressure and slower current during the hours of sleep are likely to put the finishing touch to the process.

A case reported by Eversbusch* may be merely mentioned, in which thrombosis of the central vein was supposed to have followed an injury with fracture of the upper jaw, nasal, and sphenoid bones. It is a very doubtful case (possibly of abruption of the optic nerve), not pathologically examined, and at any rate not of interest to the present inquiry. A few rare cases in which thrombosis is said to have followed upon orbital cellulitis may also be passed over as not bearing on present problems.

Among strictly local conditions favourable to, but not necessarily by themselves, causing thrombosis of the central vein, may be mentioned an unusual course of the vein itself, since it is evident that the more curved or tortuous the tube is along which the blood flows, the greater will be the friction, the greater the slowing, and the more the liability to thrombosis if the wall be diseased. There is a certain amount of proof that these considerations are of some little importance. Goh believed that in his case a thrombosis occurred in one eye and not in the other because the vein on that side took an unusually great curvature, and it will be noticed that in Case II, reported above, the vein just central to the thrombosed part took an unusual course, curving sharply away from the artery to reach the periphery of the nerve.

When all the above causes have had due weight, there

* Eversbusch, Klin. Monatsbl. f. Augenh., 1899, p 1.

still remain certain cases not easily explained. These are the cases occurring in young people without cardiac or renal disease. The cases of Purtscher and Weinbaum may be especially mentioned, which occurred in patients æt. 21 and 25 respectively, and without heart disease, arteriosclerosis, or nephritis. I have also seen a similar case in a young lady, which was further remarkable in that the hæmorrhage subsequently entirely disappeared and the vision rose to 6/6, a thing which I have not seen in any other case of true thrombosis of the main stem of the vein. These cases are not easy to account for since thrombosis in any vein is uncommon in the young, except in the two instances of varicose veins and the uterine veins after parturition, in both of which instances there are special circumstances not to be found in the central vein of the retina. Angelucci speaks of two forms of thrombosis—the marantic found in old people with angiosclerosis, and the phlebitic found in young people; but, as we have seen, Angelucci's own cases are open to the gravest suspicion as to whether they were really instances of thrombosis of the central vein, and further, his statements rest on no pathological proof. Nor is it much easier to account for a primary phlebitis in young people than to account for angiosclerotic changes. Such cases are especially worthy of pathological research as opportunity offers.

Turning now to the question why glaucoma should follow on these cases of intense hæmorrhagic retinitis, we find several explanations of the fact put forward. That glaucoma does follow oftener than can be explained on the ground of mere coincidence is a well-ascertained fact. So long ago as 1869, before thrombosis of the central vein had been described as such, v. Graefe* gave his experiences on this point, and stated that, from the number of cases in which he had seen this sequence of events, he could not regard the occurrence of glaucoma as accidental. One explanation which has been

* v. Graefe, Arch. f. Ophth., vol. xv, 1869, pt. 3, p. 184.

put forward, chiefly by Wagenmann, is that the two phenomena, hæmorrhagic retinitis and glaucoma, are really independent of one another, but are both dependent on a common cause, viz., arteriosclerosis, *i.e.*, that the vascular changes which in the posterior half of the eye resulted in hæmorrhages, in the anterior half of the eye resulted in impaired drainage and glaucoma. A little consideration of this theory will, I think, show that it is untenable. If the glaucoma is not directly dependent in some way on the hæmorrhagic retinitis, why should it attack the eye affected with hæmorrhagic retinitis rather than the other, as it undoubtedly does? v. Graefe observed 22 cases in which glaucoma followed upon hæmorrhagic retinitis. In 10 of these the other eye was unaffected after a lapse of 2 years. In 6 glaucoma followed in the other eye, but was in each case preceded by retinal hæmorrhages. In 5 the other eye was subsequently affected with hæmorrhagic retinitis, but remained free from glaucoma, and in 1 both eyes were simultaneously attacked. Presumably, on an average the amount of angiosclerosis in one eye will be much the same as in the other eye of the same person, and if the glaucoma is not dependent on the retinal hæmorrhages, but on angiosclerosis, there seems to be no reason why it should fall with greater frequency on the eye affected with retinal hæmorrhages than on the one not so affected, but the above figures show that there is no tendency for the other eye to become glaucomatous, except in consequence of the occurrence of retinal hæmorrhage in it. Again, the hypothesis that both are due to the common cause angiosclerosis does not explain cases such as those of Weinbaum, Purtscher and Wurdemann, in which hæmorrhagic retinitis followed by glaucoma occurred in young patients, since in these cases the glaucoma cannot have been due to angiosclerosis, and must undoubtedly be looked upon as a sequel to the retinal hæmorrhages. We may then fairly conclude that the two conditions are not independent, but that the glaucoma is directly the consequence on the retinal affection.

In a few cases there has been evidence of iritis (Wagenmann, Case III, Ganthier, etc.), and where this has occurred there would, of course, be an increased tendency to glaucoma, but that this is any usual explanation of these cases is easily negatived by most of the clinical histories. In Case I, given above, which was closely followed from first to last, there never was any trace of iritis. Further, it is distinctly uncommon to find any trace of inflammation in the stroma of the iris microscopically.

There are also certain instances in which glaucoma has followed upon the use of atropine (Deutschmann), but this also is quite an exceptional history in these cases, and probably indicates that the eye was already predisposed to become glaucomatous, and that the use of atropine, as it were, merely tipped the balance.

There seems then to be sufficient proof that in the majority of instances the association of glaucoma with hæmorrhagic retinitis is not a coincidence, that it is not merely a case of both being due to arteriosclerosis, but in reality independent of one another, and that it is not due in most cases to such accidents as the use of atropine or the intercurrence of iritis. We must conclude, therefore, that in some way the glaucoma is directly caused by the preceding retinal hæmorrhages. It has been supposed that in these cases there has always been a rupture of the blood through the limitans interna into the vitreous. In consequence of this, it is thought, the lens may be carried forward, bearing with it the iris and narrowing the corneo iritic angle. At the same time the nature of the fluid drained off at this angle will be altered; it will become more colloidal from admixture with the proteid constituents of the blood, and will, therefore, be less easily able to pass through the spaces of Fontana, and these two factors combined will result in increased intra-ocular tension. Some support is lent to this explanation by the fact that in many instances, with the onset of glaucoma, the media become too opaque to be illuminated, and it is also undoubtedly true that blood has actually been found in the

vitreous in some of these cases. It was present in Case III, and probably in Case II, reported above. No doubt it is the case that the presence of blood in the vitreous will increase the tendency to glaucoma, but it is quite certain that glaucoma may also occur without any trace of such vitreous hæmorrhage. In Case I, for instance, there was certainly no blood in the vitreous 9 days before the eye was obtained, and none was found on bisecting it after excision, so that it may fairly be assumed that none had occurred, and the opacity of the media in this case must be attributed mostly to œdema of the cornea.

It is, however, possible that, without actual hæmorrhage into the vitreous, the lymph currents drained at the corneo-iritic angle may still be altered in the manner indicated by the presence of profuse retinal hæmorrhages and retinal venous obstruction. It is to be remembered that the canal of Stilling is capable of being injected from the lymph spaces around the central vessels (Leber*), which shows that venous (and therefore lymphatic) obstruction in the nerve may alter the constitution of the lymph currents in the vitreous.

Such an alteration in the lymph currents may be the explanation of the onset of glaucoma in these cases, but is not the full explanation of its continuance. We have not merely to do with the drainage of abnormal lymph through normal passages, for already on the seventh day, as we see in Case I, there is a certain amount of blockage of the corneo-iritic angle by fibrous tissue—the apposition has become an adhesion—and this is a condition which constantly increases the longer the glaucoma persists. It is to be remembered also that glaucoma does not follow in every case of thrombosis of the central vein. I know of one case (shown me by Mr. Hancock) in which repeated vitreous hæmorrhages have occurred under observation, which has yet lasted 3 years without the occurrence of glaucoma. So that possibly the imperfectly understood factors which predispose to ordinary

* Leber, Graefe Saemisch Handbuch, 2nd edit., pt. 1, vol. ii, chap. XI, p. 84.

primary glaucoma play a part, *e.g.*, general smallness of the eye, shallowness of the anterior chamber, relative largeness of the lens, and angiosclerosis. It is to be remarked, however, that in Case I the anterior chamber was not shallow, but rather deep, though whether that is a common condition in cases of this kind I do not know. Angiosclerosis is probably an important factor in these cases, not as an independent cause of glaucoma according to Wagenmann's explanation, but as the predisposing cause which makes the drainage fail when the abnormally constituted lymph attempts to pass through the filtration angle.

We come now to the difficult question, What is the nature of the changes in the vessels described and figured in the foregoing account? Are they all of one kind, the different appearances being different stages in one process, or is there more than one kind of pathological change which the central vessels may suffer? Further, are the changes in the arteries of the same nature as the changes in the veins? In the first place, a few words may be said as to the peculiarities in structure of the central vessels and their retinal branches, and more particularly as to the elastic tissue in their walls, since the staining of this elastic tissue by special methods, and especially by Weigert's elastic tissue stain, has given much information recently both with regard to the normal structure of the vessel walls and with regard to the seat of pathological changes in them. It has also been of much service in distinguishing, in the case of the retinal vessels, which are arteries and which veins, a distinction by no means easily made when they are pathologically altered. The central artery, then, as far as the lamina, has the normal structure of a small arterial twig—an endothelial lining, a very narrow sub-endothelial layer, a well-marked crenated elastica interna, a relatively thick muscular coat with scanty elastic fibres, and a connective tissue adventitia fading indefinitely into the surrounding connective tissues, and containing an abundance of irregularly disposed fine elastic fibres. So far, there is nothing peculiar, but, just as the

artery passes through the lamina cribrosa, there is a change. There ceases to be any definite single crenated membrane, and its place is taken by an entanglement of fine elastic fibres, which still separates media from endothelium. Following the arteries further into the periphery of the retina, this elastic tissue soon becomes less, and in the smallest twigs seems to disappear. The wall of the central vein is composed almost entirely of fine connective tissue, only a very few cells being present, which resemble muscle cells. This fibrous tissue has no clear outer boundary, but shades off into the surrounding connective tissue quite indefinitely. It contains tolerably abundant irregularly disposed elastic fibres, which are very variable in amount, and apparently increase, as Hertel has shown, with advancing age. Sometimes these are so abundant, and so regularly arranged in a transverse direction, as to simulate a crenated membrane, more especially when the vein is collapsed and thrown into folds, but I have never been able to persuade myself of the existence of a true membrane in the vein like the crenated membrane of the artery; the high power always shows that we are really dealing with a close feltwork of fine fibres, an appearance which is not given with any power by the true crenated membrane of the artery. The distinction between intima and media is, therefore, much less distinct in the vein than in the artery, indeed, the intima seems to consist of little more than the endothelium, with, perhaps, a little sub-endothelial tissue. On reaching the lamina cribrosa, the elastic tissue of the vein wall blends with the elastic tissue of which the lamina is mainly composed; and within the lamina, so far as I have observed, there is no elastic tissue in the vein wall, and we have, therefore, in Weigert's elastic tissue stain a valuable means of distinguishing artery from vein, when the ordinary means—the wider calibre, extreme thinness, and lack of muscular tissue in the wall—fail us in consequence of pathological changes. It is well known, of course, that there is no muscular tissue in the walls of the

retinal veins. I believe that the above will be found universally true, but my observations are still somewhat scanty, and more research is needed finally to establish some of the points.

Turning now to the present series of cases we have not much difficulty in defining the seat of the pathological change in the arteries. A glance at fig. 5 will show, even without Weigert's special stain, that the intima is the part affected, and since the lumen is still lined with a tolerably even layer of endothelium it is probable that the seat of change is the sub-endothelial tissues, though it is not entirely excluded that the endothelium itself may have become proliferated while still presenting an even layer to the lumen. Weigert's elastic stain shows this even more clearly by defining the elastica interna (fig. 11), and further shows that among the proliferated cells there are numerous very fine elastic fibres which form imperfect crenated membranes within the true one, reaching each a part of the way round the lumen, but none entirely round. Within the lamina cribrosa the changes in the arteries are similar. They affect the intima (fig. 1), and seem to consist chiefly of proliferation of the endothelium.

In Case I the changes in the central vein are also undoubtedly in the intima (fig. 3). They are in the form of a clear-looking ground worked with scanty oval nuclei, and are within the area of the curly elastic fibres of the media and adventitia. Changes such as are shown in Case III (fig. 10), however, seem to involve also the connective tissue wall of the vein. The thickening is very great, there is a certain faint fibrillation in the groundwork, and Weigert's elastic tissue stain shows a very few faint elastic fibres. The endothelium shows but slight sign of proliferation. The changes in the retinal veins are probably usually of this kind. For instance, in the vessel shown in fig. 2, which has already been shown to be a vein, we have probably both endothelial proliferation and thickening of the connective tissue wall.

The terms "hyaline thickening" and "hyaline degeneration" have apparently been used somewhat loosely by authors to represent any thickening of the retinal vessel walls of more or less homogeneous aspect. They should, I think, be used only for those cases in which there is evidence of molecular impaired vitality in the tissues, in the form of loss of fibrillar structure in connective tissues, and of lost or much impaired nuclear staining. On this standard none of the changes just spoken of should be termed "hyaline degeneration," for in spite of the somewhat homogeneous ground substance in some instances (fig. 3), the nuclear staining is well preserved. "Fibrosis" would be a more proper term for the changes shown in fig. 3, and they are no doubt to be looked upon as a preservative tissue reaction against abnormal circumstances in the circulation, a strengthening of the vessel wall against undue strains. Some of the vessels in these sections do, however, show a change different from the above. They are mostly small vessels, have a homogeneous glistening aspect, and show no, or very scanty, nuclear staining. To these the term "hyaline degeneration" may be fairly applied without committing ourselves to any statement as to the exact nature of the change, and as to whether it was a primary affection of the vessel wall or followed on the fibrosis above mentioned.* What the chemical nature of this change is seems to be quite uncertain; indeed, the different names applied to it—"hyaline," "colloid," "amyloid," "mucoid"—might lead one to suspect as much. I have tried to colour this substance with the stains for amyloid disease (on hardened material, however), and also with those for mucin, but have never obtained any result. It stains pink with v. Gieson's fluid.

It seems probable then, that more than one type of change may be present in the retinal vessels. We may

* An example of what may be regarded as true hyaline degeneration in the retinal vessel walls will be found described and figured by Mr. Spicer and Mr. Parsons in the Trans. Oph. Soc., 1902, p. 306, Pl. XXII, fig. 1, p. 310.

have the intima taking the chief part as in the arteries in Case I, and in the vein far back in the nerve in the same case. To this the terms "endarteritis" or "endophlebitis" may be fairly applied if we keep clearly in mind that there is no evidence of inflammation in the ordinary sense (round cell infiltrations or cicatrisation), but merely of proliferation. Then again we may have the connective tissue of the wall playing the chief *rôle* as, for instance, in the vein in Case III, central to the obliterated portion (fig. 10). To this the terms "arteritis," "periarteritis," "phlebitis," and "periphlebitis" may be applied, again keeping in mind that there is seldom much proof of inflammation. We may also of course have combinations of these two conditions as in the retinal veins in Case I. In addition to these forms we may have, whether as a primary disease of the vessel wall or as a consequence of such changes as the above, the condition known as hyaline degeneration. We may also have the appearances produced by the organisation of thrombi within the vessel lumen, but this, of course, is not a primary disease of the vessel wall.

It is likely that such thickenings of the vessel wall do not lead to hæmorrhage at the actual point of thickening. The wall will be rather strengthened at this point, for there is no reason to think that the new-formed substance is any weaker than the original wall. The hæmorrhages are no doubt produced by the damming back of the blood owing to the narrowing of the lumen, and by the giving way either of unthickened veins more peripherally, or of capillaries which are incapable of much thickening.

The question has been more than once raised how much of the condition of the vessels described above was primary, *i.e.*, was present before any hæmorrhages or dimness of vision had occurred, and how much was secondary to impeded venous flow from thrombosis and glaucoma, and to the general prejudicial effects of continued high tension on the intra-ocular structures. Some observations by Hertel* are of

* Hertel, *loc. cit.*

importance in this connection. Struck with the difficulty just mentioned of telling primary from secondary lesions where a hindrance to the ocular circulation has lasted for some time, Hertel examined microscopically seventeen eyes from persons who had general arteriosclerosis, but no ophthalmoscopic evidence of angiosclerosis, and also a number of eyes from persons who had neither general arteriosclerosis nor ophthalmoscopic changes. He describes two kinds of change. Firstly, an increase of the elastic tissue of all the coats of the vessels, with a tendency to splitting of the elastica interna into more than one layer, but without any definite narrowing of the lumen of the vessel. Secondly, localised bulgings into the lumen consisting chiefly of proliferated endothelial cells with new-formed elastic fibres among them, and proliferation of the sub-endothelial tissues. The first of these changes he regards as not truly angiosclerotic, but merely senile, because in the examination of normal eyes of different ages he found a very definite increase in the elastic tissues from childhood to manhood, and, to a less degree, from manhood to old age (a fact which a few observations of my own tend to confirm). The second group of changes Hertel regards, however, as really pathological, and as being the changes which precede and produce the retinal hæmorrhages of old people. An interesting point in his observations is that he found these changes tolerably advanced in eyes which showed no evidence whatever ophthalmoscopically of any vascular disease. Hertel dealt chiefly with the arteries, but there is no doubt that such changes also occur in veins. Figs. 1, 2, and 3 from Case I show very extensive disease in retinal veins, yet hæmorrhages had only been present for 3 weeks, and glaucoma for 1 week. It is probable, therefore, in this case that there had not been time for the development of any very extensive changes in the retinal vessels, and that the condition shown in these figures approximately represents the condition present while the eye was still a normally functionating organ.

In conclusion, I have to thank the following gentlemen

for gifts of material, and for permission to use cases under their care, viz., Mr. Treacher Collins for Cases I and III, Mr. Simeon Snell for Case II, Mr. Percy Flemming for Case IV. I have also to thank Mr. J. Herbert Parsons for the use of the hospital's excellent microphotographic apparatus.

Description of Plates.

Case I.

Fig. 1.—A small artery and vein on the papilla, stained with Weigert's elastic tissue stain × 120. The artery is the vessel to the right. Abundant elastic tissue in its wall, within which proliferated intima is seen, greatly and eccentrically narrowing the lumen. Vein has extremely thick wall and narrow blood-filled lumen, and fails to take on elastic tissue staining.

Fig. 2.—A retinal vein × 120. Wall enormously thick and lumen very small. Inner layer more granular and with more abundant rounded nuclei; outer more homogeneous and with scantier, more elongated nuclei. Dilated circumvascular lymph spaces. Coagulated exudate in retina. Membrana limitans interna unbroken.

Fig. 3.—A portion of the central vein within the nerve, stained with Weigert's elastic stain × 200. Many wavy elastic fibres in the wall, but no true crenated membrane. Within this, thick proliferated intima with scanty pale nuclei. The lumen lined with a fairly even layer of endothelium. A little piece of the arterial wall is also seen.

Case II.

Fig. 4.—Thrombus in a retinal vein × 100. Large rounded mass with scattered groups of nuclei, separated from surrounding tissues by a cleft for about two-thirds of circumference, connected by nucleated, young connective tissue in the remaining one-third. Limitans interna intact, bulged towards vitreous. Internal nuclear layer bowed outwards. Abundant hæmorrhage in retina. Small artery out of focus to right.

Fig. 5.—Central vessels × 120. Artery shows endarteritis—the crenated membrane can be seen outside the eccentric nucleated thickening of the intima. Lumen lined with intact endothelium. Vein of normal size. Lumen divided into loculi containing blood, by thin trabeculæ continuous with tissue of wall and lined by endothelium. No cellular infiltration of surrounding tissues.

FIG. 6.—Central vessels a few sections central to last × 120. Artery as before. Little piece of organised tissue in centre of lumen of vein, lined with endothelium externally, and has in its centre a very small lumen also containing blood and lined with endothelium. Main lumen of vein contains blood, and has also a layer of endothelium. A small twig is entering from the surrounding trabeculæ.

CASE III.

FIGS. 7 to 10 show sections in order from before backwards, but all the sections of the series are not reproduced. The central vein on the tissue in its position is in each case at the top of the figure.

FIG. 7.—Central vessels × 170. Artery contains blood, has large lumen, and shows no endarteritis. Vein lumen rather small, but no endothelial proliferation. Contains a homogeneous coagulum, whose edges are infiltrated with leucocytes, while its centre remains free. No blood in rest of lumen. Surrounding tissues condensed.

FIG. 8.—Central vessels × 170. Arterial lumen smaller. Vein represented by a little knot of cellular new-formed connective tissue with, however, a trace of the old lumen left at each end of it. No infiltration of surrounding tissues

FIG. 9.—Central vessels × 170. Artery shows some endarteritis. Position of vein represented by the somewhat more cellular connective tissue at the top of the figure. Into this tissue a very small vessel is seen entering. On the other side of the artery is a collateral vein, which has come in from the trabeculæ of the nerve, and has turned back to accompany the artery. It will subsequently cross to the other side of the artery and help in the restoration of the lumen of the vein. It contains some coagulum infiltrated with leucocytes and plastered up against one wall.

FIG. 10.—Central vein × 170. A narrow lumen has been restored, and now contains not coagulum, but formed blood corpuscles, showing that an active circulation was going on in it. The wall is extremely thick, has a faint fibrillar structure, and shows scanty nuclei. The vein has separated a little from the artery, only a small portion of which is shown.

FIG. 11.—The central artery stained with Weigert × 90. Very thick crenated membrane. Within this a fine feltwork of new-formed elastic fibres, which at one place is separated from the crenated membrane by a clear area in which blown-out and vacuolated cells are found. The vein is obliterated at this spot; the place where it should be is towards the top of the figure.

CASE IV.

FIG. 12.—Central vessels at level of lamina cribrosa × 100. Artery, somewhat obliquely cut, is filled with coagulum and red blood corpuscles. There is no vein, unless the little slit in the connective tissues to the right represents it.

FIG. 13.—Central vessels a few sections farther back × 100. The coagulum in the artery has shrunk somewhat and pulled away the crenated membrane—a *post-mortem* appearance. Two little venous twigs are joining to re-form the central vein (a little septum will be noticed between them). These twigs are filled with well-formed blood corpuscles.

FIG. 14.—Central vessels far back in the nerve × 100. The artery is small and shows much endarteritis. Within its lumen there is an organised cellular plug, separated from the proliferated intima by a cleft in which there are some red blood corpuscles. The crenated membrane is faintly visible outside the thickened intima. The vein lumen is quite restored by the accession of collaterals.

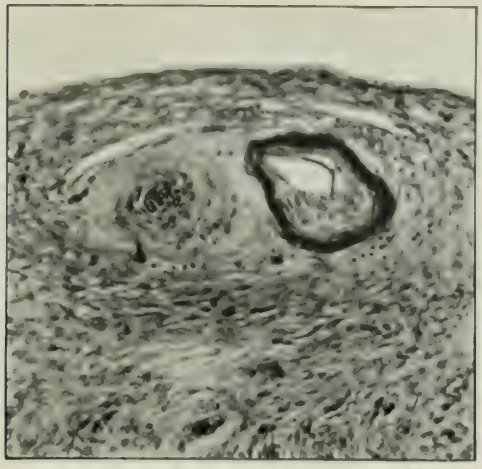

FIG. 1. x 120.

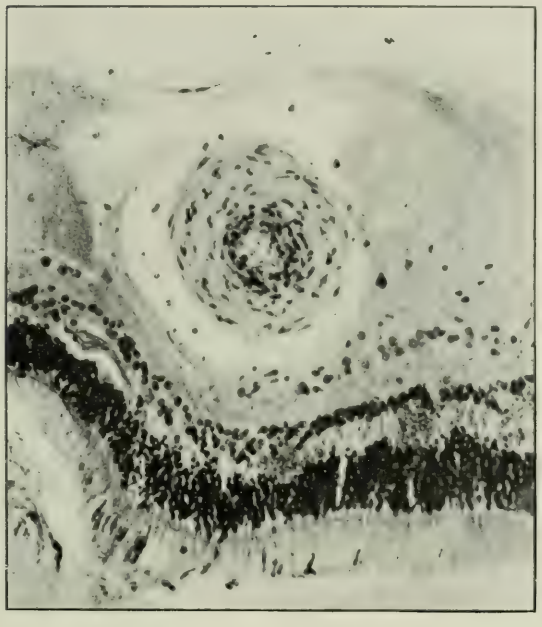

FIG. 2. x 120.

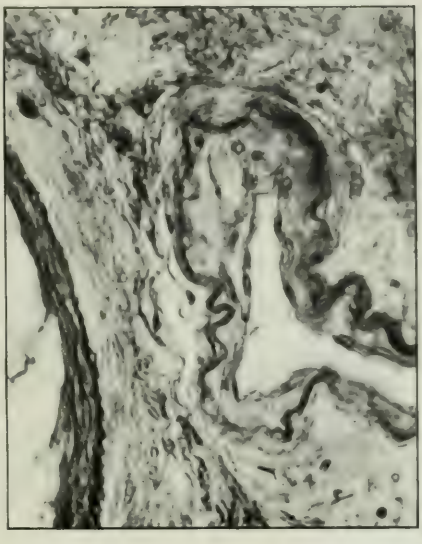

FIG. 3. x 200.

FIG. 4. × 100.

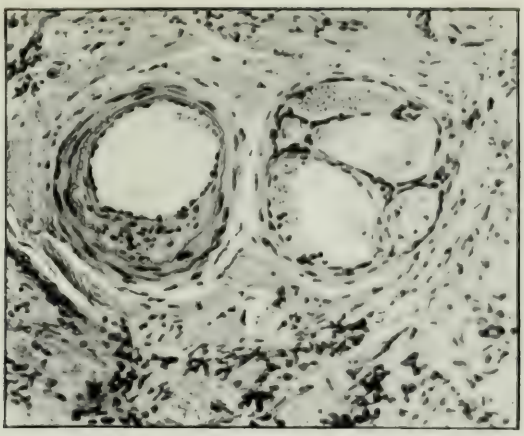

FIG. 5. × 120

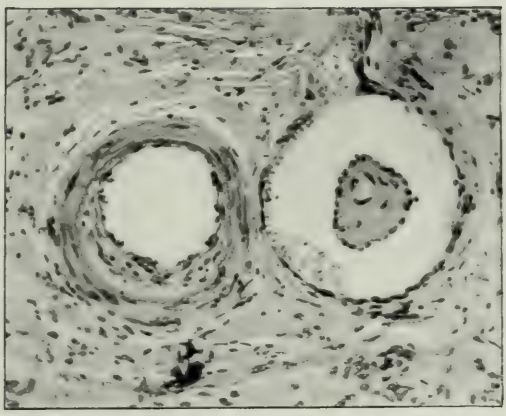

FIG. 6. × 120.

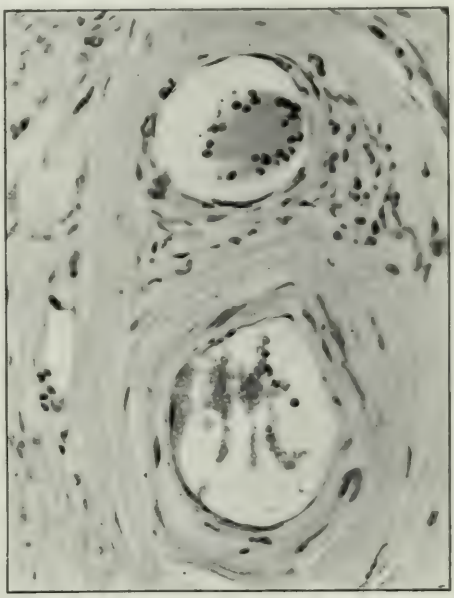

FIG. 7. × 170.

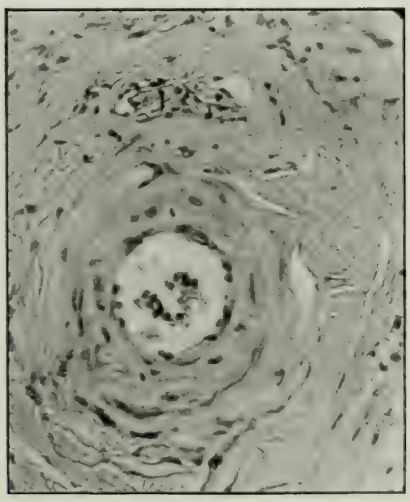

FIG. 8. × 170.

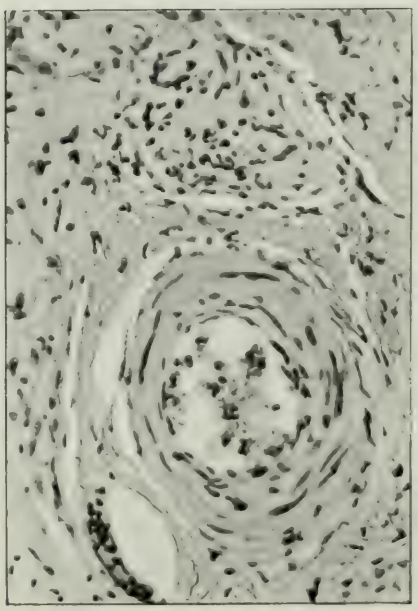

FIG. 9. × 170.

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FIG. 10. × 170.

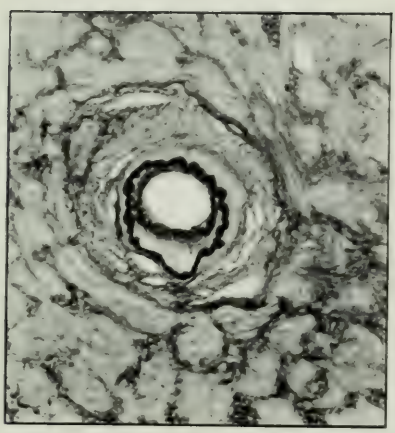

FIG. 11. × 90.

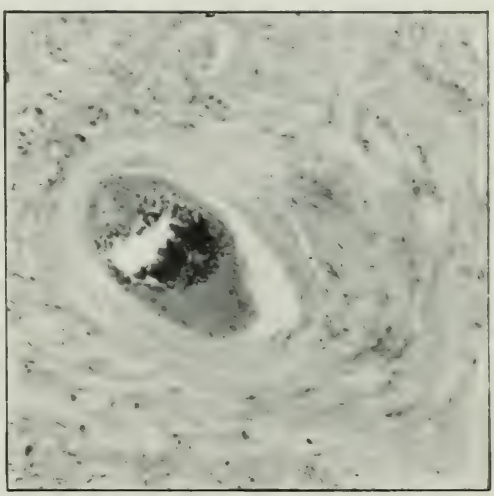

FIG. 12. × 100.

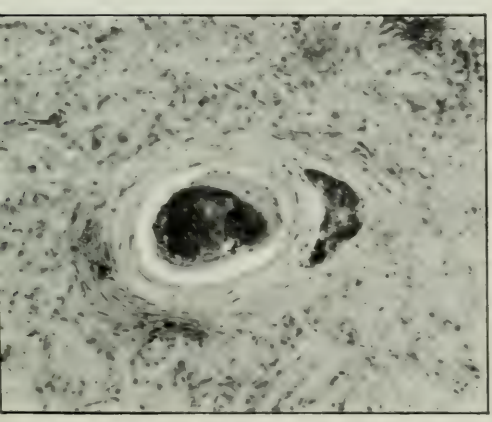

FIG. 13. × 100.

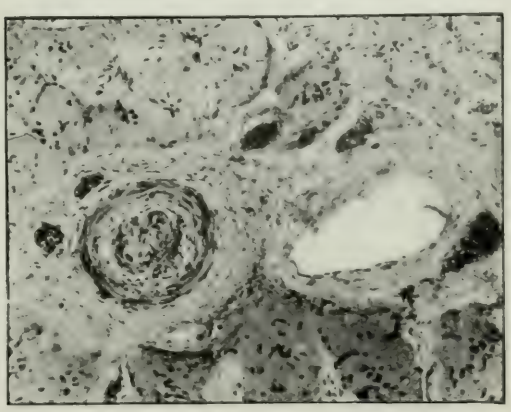

FIG. 14. × 100.

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The Royal London

Ophthalmic Hospital Reports.

Vol. XVI. Part II. March, 1905.

ON THE DEVELOPMENT OF THE ACCOMMODATIVE POWER OF THE HUMAN LENS.*

By E. Treacher Collins.

The accommodative power of the human lens was demonstrated by Helmholtz to be due to its elastic fibres being maintained in a state of tension, the relaxation of which brought about an increased convexity of its anterior surface. The way in which this state of tension of the lens fibres is developed forms the subject of this paper.

The relaxation of the tension of the lens fibres in accommodation was stated by Helmholtz to be effected by slackening of the suspensory ligament of the lens, and this theory, though contested by some, is supported by much clinical and experimental evidence. The development of the accommodative power of the lens must be looked for, therefore, in the development of its suspensory ligament.

In a paper on that subject published in vol. xiii, pt. 1 of these reports, I gave a table showing the diameter of a series of eyeballs and their lenses from the 4th to the 9th month of fœtal life.

At the 4th month the ciliary body is in contact with the

* This paper was read at the Tenth International Congress of Ophthalmology held at Lucerne. It is republished here, together with illustrations not previously reproduced. These illustrations are from photo-micrographs kindly taken for me by Mr. E. Collier Green, of Derby.

sides of the lens. At the 9th month the transverse diameters of the eyeball and the lens are double what they are at the 4th month, and in the adult they are treble what they are at the 4th month. As the eyeball and lens increase in size in this proportion, and as the eyeball is larger to begin with, it follows that as the eye develops there must be a gradual separation of the ciliary body away from the sides of the lens.

It is natural to suppose that the adhesions which join the lens to the ciliary body, viz., the fibres of the suspensory ligament, would be first formed while those structures are in contact, and that they would be stretched out and rendered tense as they become separated.

Sections of a human fœtal eye in which, what ultimately develops into the *pars ciliaris retinæ* is in contact with the lens, show, intervening and lying in contact with both, some tissue composed of spindle shaped cells of mesoblastic origin (Pl. II, Fig. 1).

In this tissue is subsequently developed the network of blood vessels which forms a vascular sheath to the lens.

In sections of fœtal eyes of a later date where the rudimentary ciliary body has become separated from the sides of the lens, in the situation of the suspensory ligament elongated cells may sometimes be seen, or fibres of the suspensory ligament with nuclei attached to them (Pl. IV, Fig. 1).

Similar elongated cells or fibres with nuclei on them are met with in congenital microphthalmic eyes in the situation of the suspensory ligament, evidently due to its arrested development. These malformations are referred to again more in detail at the end of this paper.

There seems then considerable evidence to show that the suspensory ligament of the lens is originally derived from cells which become lengthened out into fibres and lose their nuclei.

There are two possible sources of these cells :—

1. The mesoblastic cells already referred to as surrounding the lens capsule at a very early period of fœtal life.
2. The neural epiblastic cells composing the *pars ciliaris retinæ*.

A priori, seeing that the suspensory ligament is of the nature of a connective tissue it would be natural to suppose that it was derived from mesoblast. Its intimate association with the vitreous humour is also in favour of the two structures having the same genetic origin.

Schoen* and Terrien,† however, as the result of their histological researches, regard the fibres of the suspensory ligament as derived from the epithelial cells forming the *pars ciliaris retinæ*, *i.e.*, making them analogous to the fibres of Müller which form the supporting connective tissue of the retina.

I have myself been unable to arrive at any certain conclusion in favour of one or other of these views, and fortunately it is immaterial for the purpose of this paper which is ultimately found to be correct.

The most recent investigations‡ into the arrangement of the suspensory ligament in the human eye have shown that the bundles of fibres of which it is composed do not pass straight out from the sides of the lens to the ciliary body, but that they cross one another. Thus fibres which are most anterior in their attachment to the lens capsule pass to the hindermost part of the ciliary body, whilst those coming from the foremost part of the ciliary body pass to the posterior part of the lens capsule.

It has been possible to differentiate several groups of fibres and describe them by distinctive names. Thus, the fibres which pass from the non-plicated part of the ciliary body to the anterior part of the lens capsule, and which lie in the valleys between the ciliary processes, are called *the orbiculo-antero-capsular fibres.* Those which pass from the *ora serrata* and the hindermost part of the non-plicated part of the ciliary body to the posterior part of the lens capsule are *the orbiculo-postero-capsular fibres.* Those passing from the apices of the ciliary processes to the posterior part of the

* Anatom. Anzeiger, Bd. x, 1895.

† Archives d'Ophtal., T. xviii, 1898, p. 555.

‡ Garnier, Archiv f. Augenheilk., Bd. xxiv, 1892.

lens capsule, between the bundles of the orbiculo-antero-capsular fibres, are *the cilio-postero-capsular fibres;* and those running directly inwards from the ciliary processes to the lens capsules are called *the cilio equatorial fibres.* (Pl. I, Figs. 1 and 2).

Some writers have also described certain *accessory fibres* passing from the non-plicated part of the ciliary body to the ciliary processes, from one ciliary process to another, or from the ciliary body to adjacent fibres. It is very possible, however, that these so-called accessory fibres are really only some of the other bundles of fibres cut obliquely.

In order to understand how this interlacement of the different bundles of fibres of the suspensory ligament is brought about, it is necessary to examine the relation which the different parts of the ciliary body bear to the sides of the lens at different periods in fœtal life. When the lens vesicle is first formed and has become cut off from the surface epiblast there is no ciliary body and no iris. The anterior extremity of the optic vesicle at that time corresponds to what afterwards becomes the *ora serrata,* and it lies in contact with the antero-lateral portion of the newly formed lens vesicle. (Pl. II, Fig. 1).

As the iris and ciliary body bud out of the anterior extremity of the secondary optic vesicle and the anterior extremity of the rudimentary choroid, that part of the retina which corresponds ultimately to the *ora serrata* gets displaced backwards along the side of the lens, until, from being in contact with the anterio-lateral part of that structure it comes to lie in contact with the posterio-lateral part. (Pl. II, Fig. 2).

At first the ciliary body has no ciliary processes, at that time being represented only by a short straight unfolded area lying in close apposition with the sides of the lens.

Folds commence to bud out from the ciliary body at its anterior extremity, *i.e.*, where it joins the rudimentary iris. These folds extend inwards and backwards, passing between the side of the lens and the unfolded area of the ciliary body,

which by that time have become somewhat separated. The apex of these folds extends so far back along the side of the lens as to reach its posterior lateral parts. (Pl. III, Fig. 1.)

In the later growth of the eye both plicated and non-plicated parts of the ciliary body become separated away from the sides of the lens. The development of the anterior chamber, and consequent displacement backward of the lens, tends still further to draw the ciliary processes away from a level with its posterior surface to a level with its anterior surface. (Pl. III, Fig. 2.)

The final stage in the development of the ciliary body, and one which is not complete until some time after birth, consists in the lengthening out of the non-plicated part of the ciliary body, and the further displacement backwards of it and of the *ora serrata* away from the lens. (Pl. IV, Figs. 1 and 2.)

It will thus be seen that different portions of the ciliary body are in contact with the sides of the lens at different times, and that adhesions which form between them must originate at different times.

The first to be formed are those passing between the anterior part of the lens capsule and the non-plicated part of the ciliary body, which as these structures grow apart become stretched out into the orbiculo-antero-capsular fibres of the suspensory ligament.

Next in formation are the adhesions between the posterior part of the non-plicated part of the ciliary body, together with the *ora serrata*, and the posterior part of the lens capsule which later result in the orbiculo-posterio-capsular fibres.

As the ciliary processes commence to form and grow, extending backwards between the rudimentary non-plicated part and side of the lens, they pass between the several bundles of the orbiculo-antero-capsular fibres, which latter come ultimately to lie in the valleys between the ciliary processes.

While the ciliary processes lie in contact with the sides

and posterior lateral portion of lens, adhesions form, which on separation of those structures become lengthened out into cilio-posterio-capsular fibres and cilio-equatorial fibres.

The growth of the ciliary body away from the side of the lens, not only tends to stretch out and lengthen adhesions which have formed between them, but also causes considerable traction on the capsule of the lens.

We find that in early fœtal life, when the ciliary body is in contact with the lens the latter is round. As the ciliary body grows away from it, its lateral diameter increases considerably out of proportion to its antero-posterior diameter.

If this lateral traction on the lens is exerted to an abnormal extent, as it is in the expansion of the ciliary region in buphthalmic eyes, then the disproportion between its lateral and antero-posterior diameters becomes markedly increased.

The growth of the ciliary processes away from the posterior lateral portion of the lens, and the displacement of the lens backwards on the formation of the anterior chamber causes, through the cilio-posterior capsular fibres, considerable traction on the posterior capsule (Fig. *a* in text).

The growth backwards away from the sides of the lens of the non-plicated portion of the ciliary body causes, through the orbiculo-antero-capsular fibres, considerable traction on the anterior capsule.

There are thus developed in the growth and expansion of the eye forces dragging on the posterior part of the lens capsule forwards and outwards, and on the anterior part of the lens capsule backwards and outwards.

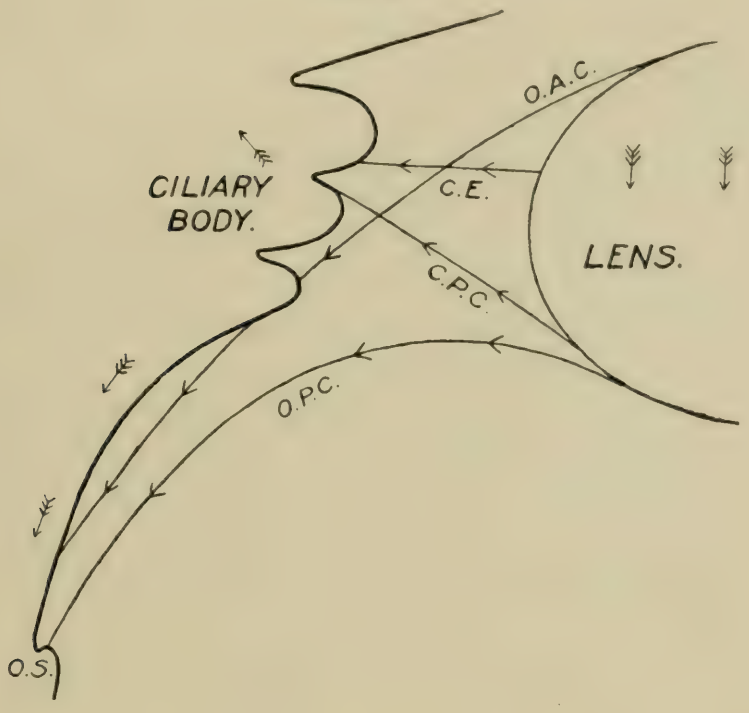
The effect of this on the elastic curved lens fibres is to cause them to become more bent and kept in a state of tension. A state of tension which is only relaxed when by the contraction of the ciliary muscle the suspensory ligament is slackened and the pull on the capsule relieved.

It is interesting to note, in connection with the development of the ciliary body in the human eye, that the different temporary stages through which it passes are

formed as permanent conditions in lower animals. In the lowest fish, eels, and also in some species of carp, there is no ciliary body, the retina ends at the base of the iris. (Pl. V, Fig. 1).

In the following teleostean fish, whiting (*gadus merlangus*), cod (*gadus morrhua*), mackerel (*scomber scombrus*), and plaice (*pleuronictis platessa*), the termination of the retina does not extend quite so far forwards, it does not quite reach up

FIG. *a*.



to the root of the iris. In eels and the carp it extends as far as, or further than, the anterior margin of the cartilage in the sclerotic, in the others it is situated behind that point.

In the following elasmobranch fish, the thornback (*raja clavata*), the lesser spotted dog fish (*scyllium catulus*), and the spring dog fish (*acanthus vulgaris*), the displacement backwards of the anterior termination of the retina is still more marked. The area which extends between it and the root of the iris is thrown into shallow folds laterally, and has

some slight elevations and depressions antero-posteriorly. It is lined by a single row of unpigmented cells, the *pars ciliaris retinæ*.

In the eyes of the following reptiles, the land tortoise (*testudo Græca*), the slow worm (*anguis fragilis*) and the sand lizard (*lacerta agilis*), the ciliary body is represented by a short area lined by a single row of unpigmented cells, situated between the root of the iris and termination of the retina without any elevations or depressions in it. (Pl. V, Fig. 2). In the common ringed snake (*coluber natrix*) there is a well marked simple fold protruding inwards and backwards in the ciliary region, lined by columnar shaped unpigmented cells. (Pl. VI, Fig. 1.)

All mammals, including the ornithorrynchus and echidna, have well marked ciliary processes showing in antero-posterior sections well developed folds. The amount of plication of the ciliary processes varies considerably in different species, but in all except the quadrumana the extent of the non-plicated area is markedly less than in man.

The following table shows that the distance between the root of the iris and the *ora serrata* compared to the antero-posterior diameter of the globe is greater in the quadrumana and man than in other mammals. That is to say, that in those mammals who have greatest amount of accommodative

	Antero posterior diameter of eyeball.	Distance between root of iris and ora serrata.
	mm.	mm.
Man	24·8	6
Chimpanzee	19	4·25
Rhesus monkey (India)	19·5	5
Capuchin monkey (South America)	18·5	4·25
Cat	22	3·5
Sheep	28	6
Bullock	35	6·5
Pig	22	4
Rabbit	19	2

power, there is the widest separation of the *ora serrata* from the anterior surface of the lens and consequently the greatest amount of drag on the anterior capsule.

In the examination of sections of human microphthalmic eyes it is frequently found that there has been an arrested development of the ciliary body and suspensory ligament.

Relations of the ciliary body to the sides of the lens which are only temporary phases in fœtal life are found, and evidence of the cellular origin of the fibres of the suspensory ligament is met with.

In one microphthalmic eye of which I have recorded a description, the vascular system of the vitreous and lens, which exists during fœtal life, had failed to become obliterated, a complete network of blood-vessels encircled the lens. The ciliary processes had failed to develop, the *pars ciliaris retinæ* and *ora serrata* were in contact with the sides of the lens. In the expansion of the globe their adhesion to the lens had remained so firm, that the two layers of the secondary optic vesicle became torn apart in the ciliary region, instead of its inner layer growing away from the lens. In other microphthalmic eyes, where the central hyaloid artery has remained patent and where the anterior part of the vitreous has developed atypically, I have found the ciliary processes passing backwards and adherent to the posterior lateral part of the lens.

I have also found that the retina at the *ora serrata* has failed to grow backwards away from the back of the lens, a fold having become formed in it in that position. An abnormally short non-plicated area of the ciliary body is a frequent accompaniment of microphthalmia.

I have sections of microphthalmic eyes in which the apices of the ciliary processes are in close proximity to the lens capsule, and where some elongated cells join the two structures. Also sections of several eyes in which stretching between the ciliary body and the lens capsule are fibres, like those of the suspensory ligament but with nuclei on them. Some of these at their insertion into the ciliary body are seen

to pass definitely into elongated cells (*vide* Figs. 1 and 2, pp. 84 and 85, vol. xiii, of the R.L.O.H. Reports).

In one specimen in which the lens was congenitally displaced, in the interval between the ciliary body and lens on the opposite side to which the latter was drawn, there were no fibres of suspensory ligament, but lying in the circumlental space in front of some atypically developed vitreous were some elongated cells and nucleated fibres. (Pl. VI, Fig. 2.)

Description of Plates I—VI.

Plate I, Figs. 1 and 2.—Show the suspensory ligament of the lens in sections of a normal human eye. The foremost fibres shown in Fig. 2 are the orbiculo-antero-capsular fibres, the prolongation of which backwards to the non-plicated part of the ciliary body is shown in Fig. 1. The hindermost fibres shown in both figures are the orbiculo-postero-capsular fibres. The cilio-equatorial fibres can be seen in Fig. 2 crossing the orbiculo-antero-capsular fibres, and passing direct from the ciliary processes to the equator of the lens. The cilio-postero-capsular fibres are shown in Fig. 2 and at their commencement in Fig. 1. They cross the cilio-equatorial and orbiculo-antero-capsular fibres, and pass to the back of the lens.

Plate II, Fig. 1.—Shows a section through the eye of a human fœtus of the 6th week. The lens vesicle has become shut off from the surface epiblast. There is no iris or ciliary body. The termination of the secondary optic vesicle touches the antero-lateral part of the lens. The ciliary body and iris grow out from it, and what is at this stage its termination ultimately corresponds to the *ora serrata*. Some tissue, composed of spindle-shaped cells which becomes the fibro-vascular sheath of the lens, lies between the sides of the lens capsule and the inner layer of the secondary optic vesicle.

Fig. 2.—Shows a section of fœtal pig's eye. The lens is in contact with the back of the cornea. The iris and ciliary body have commenced to grow out of the anterior part of the secondary optic vesicle. The part which would have ultimately corresponded to the *ora serrata* lies opposite the equator of the lens.

Plate III, Fig. 1.—Shows a section through the anterior part of a human fœtal eye of about the 10th week. The eyelids are seen united over the front of the cornea. The lens is in contact with the back of the cornea. The iris is beginning to grow and insinuate itself between the lens and cornea. The ciliary process is seen beginning to grow out with a direction backwards towards the postero-lateral part of the lens. In the preparation of the specimen the pigmented

layer of the ciliary body has become slightly separated away from the *pars ciliaris retinæ ;* the latter lies in close contact with the side of the lens.

Fig. 2.—Shows a section through a portion of a human fœtal eye of between the 4th and 5th month. The lens is separated away from the cornea, and the ciliary processes from the side of the lens. The most anterior of the ciliary processes points backwards in the direction of the posterior lateral part of the lens. A piece of a cellular adhesion, which stretched between them, is shown attached to the postero-lateral part of the lens. There is no non-plicated part of the ciliary body.

Plate IV, Fig. 1.—Shows a section through a portion of a human fœtal eye of between the 4th and 5th month. The lens is separated from the back of the cornea. The ciliary processes have grown a short way away from the side of the lens; stretching between them can be seen the fibres of the suspensory ligament with a few nuclei faintly showing on them. There is no non-plicated part of the ciliary body. The retina, in preparing the specimen, has become detached; the *ora serrata* is situated at the termination of the ciliary processes.

Fig. 2.—Shows a section through the ciliary body and suspensory ligament in a normal adult human eye. The wide separation of the *ora serrata* from the ciliary processes and from the side of the lens is seen. It is due to the lengthening out of the non-plicated part of the ciliary body.

Plate V, Fig. 1.—Shows a section through the angle of the anterior chamber and anterior termination of the retina of the eye of an eel. The posterior layers of the cornea, in the preparation of the specimen, have become spaced out. The anterior chamber is very shallow. There is no ciliary body. The anterior termination of the retina extends up to the root of the iris, almost as far as the angle of the anterior chamber.

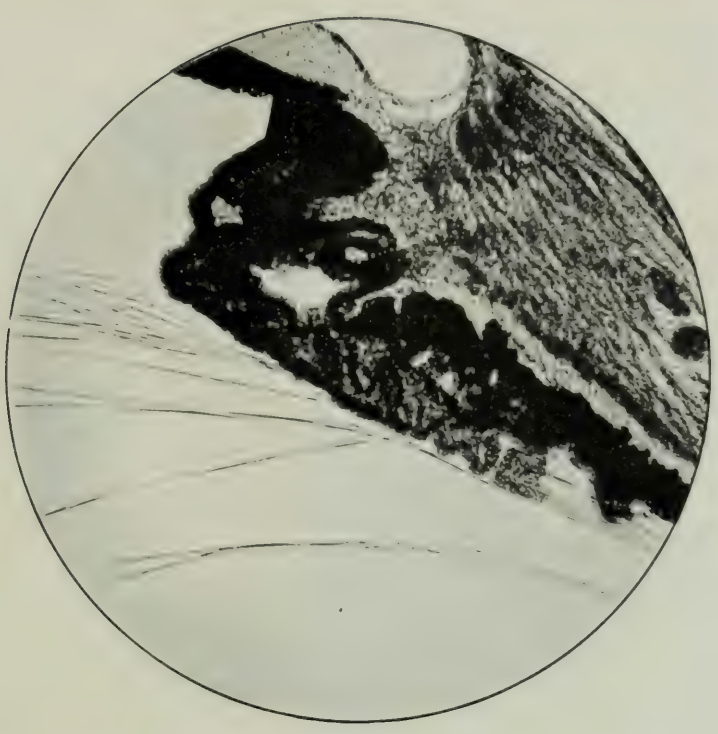
Fig. 2.—Shows a section through the eye of a sand lizard. There is a small non-plicated area seen between the root of the iris and the anterior termination of the retina.

Plate VI, Fig. 1.—Shows a section through the angle of the anterior chamber and ciliary region of the eye of a common ringed snake. The anterior chamber is very shallow. Between the root of the iris and the anterior termination of the retina one simple fold protrudes inwards, constituting the ciliary body.

Fig. 2.—Shows a section through ciliary region of a human eye which had a congenitally displaced lens. Between the ciliary processes and the side of the lens, instead of the fibres of the suspensory ligament, some elongated cells and nucleated fibres are seen.

Description of Fig. *a* in Text.

This diagram is to represent the direction of the different forces which come into play in the development of the suspensory ligament. The letters are the initials of the names of the different sets of fibres in the suspensory ligament, which are here each represented by a single line. The arrows and arrow heads show the direction in which traction is exerted on the lens. The arrows on the lens itself indicate that on the formation of the anterior chamber it is displaced backwards.



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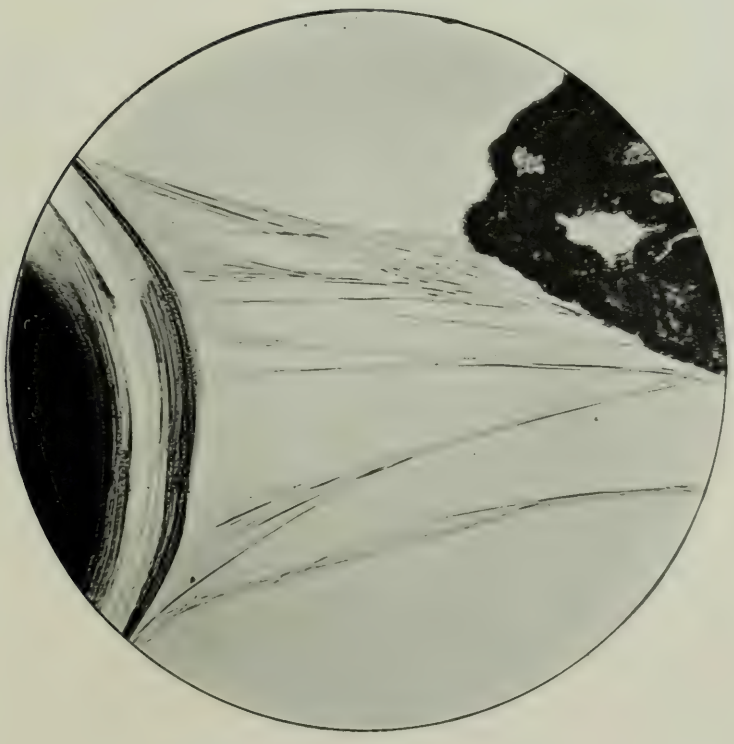

FIG. 2.

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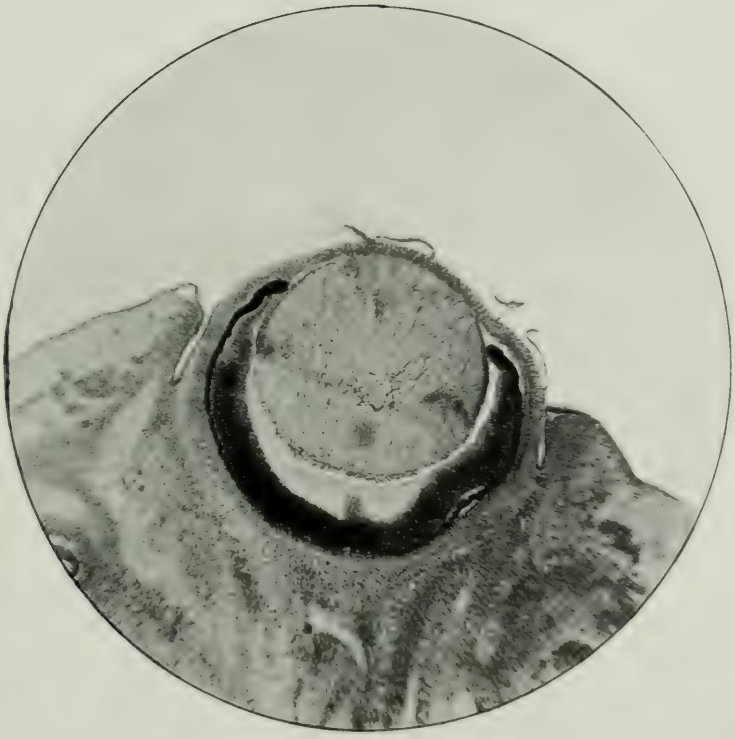

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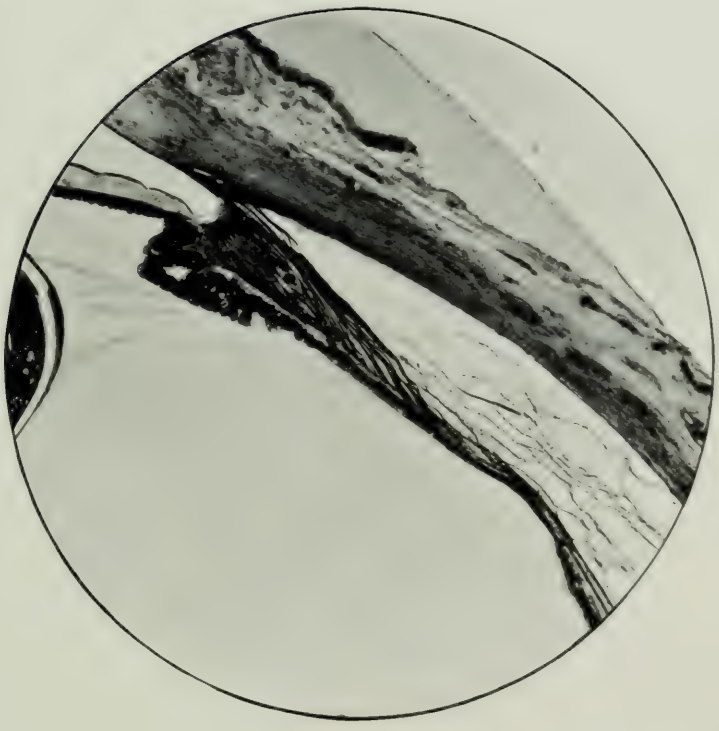

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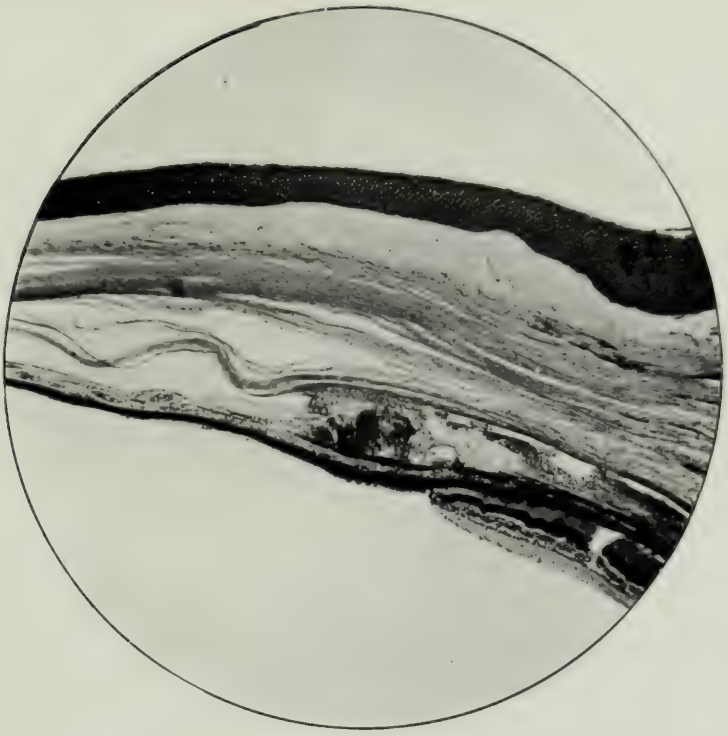

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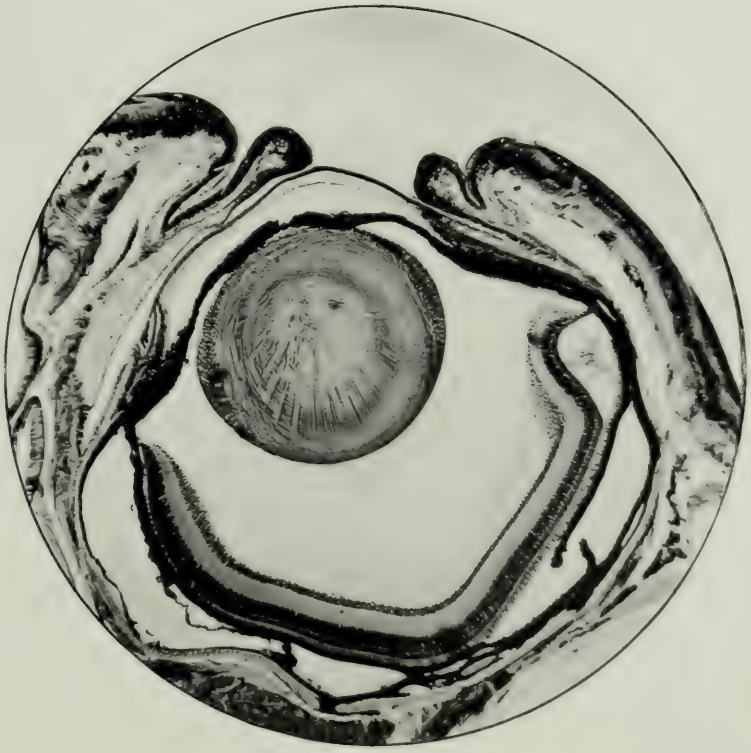

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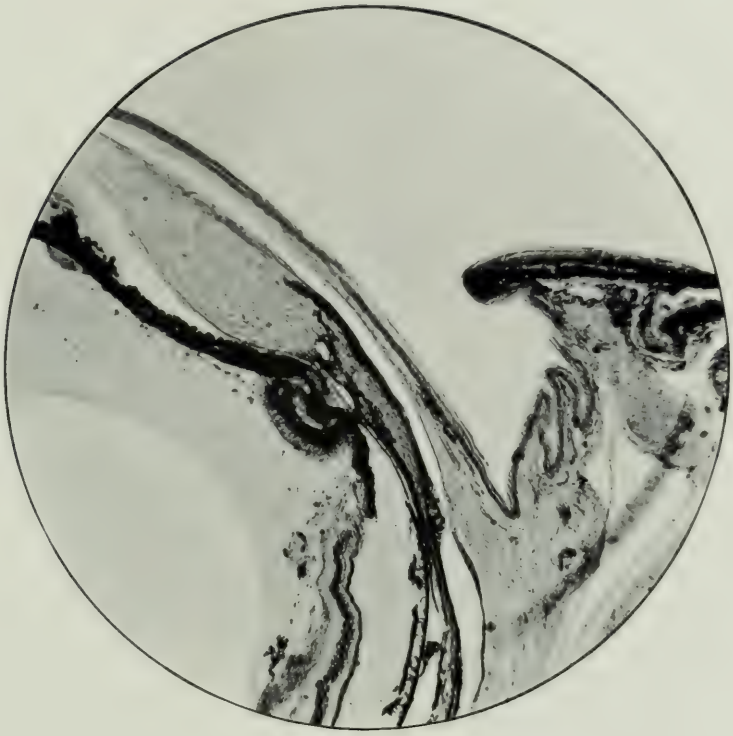

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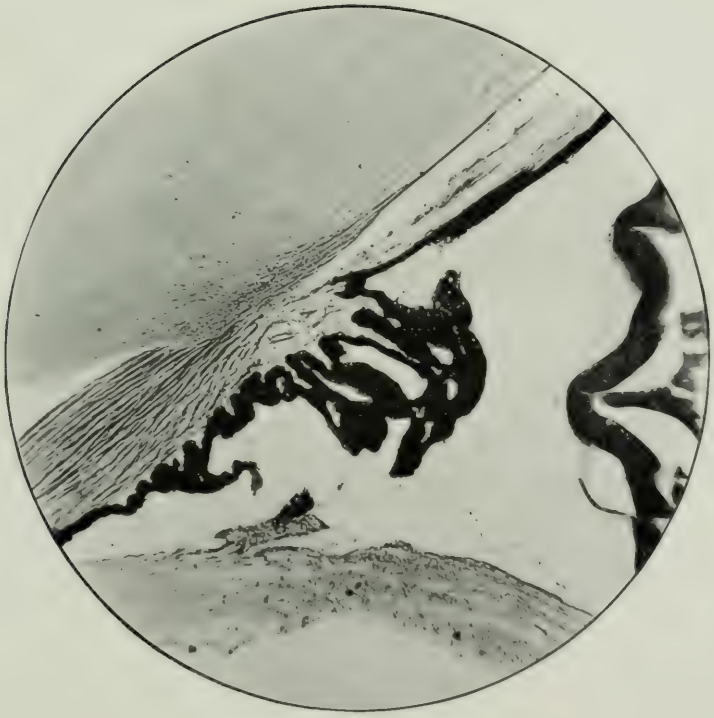

FIG. 2.

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TWO CASES OF COLLOID (HYALIN) DEGENERATION OF TARSUS AND CONJUNCTIVA.

By H. Herbert, Major, I.M.S.

With every desire to avoid contributing to the confusion that exists among hyalin and allied degenerations, the term "colloid" is here retained because, apart from the reasons given* in the description of an earlier case of conjunctival degeneration, neither of the two cases now related, nor the one just referred to, can be classed strictly as belonging either to the hyalin or amyloid subdivisions of v. Recklinghausen's colloid group. As is so often the case, the amyloid reactions obtained (in sections of fixed and hardened tissue only) were partial and incomplete.

Case I.—A Hindoo woman of 39 years. Right upper lid alone affected. Lid swollen and drooping from considerable thickening and vertical enlargement of tarsus. The maximum vertical measurement of the latter was apparently† 1·6 cm. towards its outer end. Eversion of the lid was difficult, and caused a little bleeding from a few points on the conjunctival surface. The tarsus and its covering of conjunctiva presented a yellowish, somewhat translucent appearance, except where there was a patch of opaque scar-tissue in the conjunctiva. The same yellowish tint and translucence were also noticeable in the conjunctiva for a little distance above the tarsus. A good deal of the firm wax-like tissue was removed; the knife cut into it very easily, and there was little bleeding. The conjunctiva

* (1) The fact that the same changes in the skin are known by dermatologists as colloid degeneration, and (2) the suitability of the term to define what is mainly a derivative of collagen (white fibrous tissue). See Trans. Ophth. Soc., vol. xxii, 1902.

† It was impossible to define exactly the limits of the tarsus in sections. The vertical extent here given probably therefore includes a little of the neighbouring thickened tissues.

presented no abnormality beyond the patch of scarring above mentioned, and slight papillary roughness and general injection.

CASE II.—Male Hindoo of 25 years. The right upper lid was here also the one affected; its upper part only was noticeably swollen. On eversion of the lid the upper half of the enlarged tarsus was found considerably thickened, and made up mainly of two petrified masses, covered only by conjunctiva. When the conjunctiva was divided these masses shelled out easily, their immediate surroundings being of a loose, spongy nature. The larger of the two measured 1 cm. in length and 3 mm. in thickness; the other mass was much smaller. A few microscopic spicules and strips of true bone were afterwards found in sections of the decalcified larger mass, but none in the smaller one. The neighbouring thickened tarsus had undergone colloid change, as had also the conjunctiva and subconjunctival tissues for some little distance above.

The very considerable extent of smooth swelling above could not be fully seen till after the excision of much of the enlarged tarsus. From the swollen retrotarsal conjunctiva, when incised, much soft wax-like material could be readily expressed; but the tissues were decidedly vascular, and the colloid change not sufficiently advanced to produce the semi-translucent clinical appearance so noticeable in Case I.

There was fairly advanced pannus on this side; none in the other eye. In the conjunctiva some traces of cicatricial tissue and slight thickening and papillary roughness, but no follicles; similar changes, less marked, on the other side.

A full account of the changes found in sections need not be given, but a few special points must be noticed regarding firstly the soft parts, and secondly the petrified and ossified tissues.

A. Soft Parts.

The colloid change is most advanced* in Case I, corresponding with clinical appearances. No elastic tissue can be

* The biuret reaction was readily obtainable in the colloid substance of this case, though not of Case II (the only sections tested in Case II were from the retrotarsal conjunctiva).

found in the parts examined from this Case, even in the blood-vessels, and the only remains of collagen (white connective tissue fibres) in the colloid blocks, as shown by acid fuchsin, are very blurred and indistinct; and in places (see Pl. VII, Fig. 1) there is nothing now recognisable of the conjunctiva but the epithelium, though elsewhere there is still a fairly thick adenoid layer. Tracts of cells, mostly plasma cells and cells transitional between plasma cells and fixed connective tissue cells, penetrate throughout the altered tarsus.

The results of the *tests for amyloid* are as follows:— The greater part of the colloid substance stains reddish-brown with iodine, but a few of the blocks in Case I at once acquire a pale greenish tint (!), which is not altered by treatment with dilute sulphuric acid. The acid changes the reddish-brown colour to dark brown, especially dark in Case I. In some of the much altered blood-vessels of the retrotarsal subconjunctival tissue of Case II small scattered areas (see Pl. VII, Fig. 2) within the still recognisable "internal elastic lamina" become lilac-coloured with thionin. Negative results were obtained in both cases with gentian and methyl violet, methyl green, and iodine green, used both in weak solution for 24 hours, and in strong solution.

Cellular degeneration.—Divergent views as to the part played by the cells in colloid degeneration arise from three sources: (1) the absence of distinctive staining reactions for the colloid material; (2) close contact of some degenerating connective tissue cells (and endothelial cells?) with colloid blocks; and (3) the uncertainty as to whether homogeneous material lying in cells has been merely taken up by the cells or formed in the cells.

In the adenoid layer of the retrotarsal conjunctiva of Case II where the changes are not very advanced, the breaking up of plasma cells is much in evidence. But the vacuoles seen in the cells are quite clear and unstained. Lying free among the cells there are numerous small rounded particles. Many of them display their cellular origin by colouring deeply with polychrome methylene blue; other particles

show a preference for orceïn in varying degree, and possibly indicate a change preliminary to fusion into colloid masses. The cells shown in Pl. VIII, Fig 1, are all taken from the adenoid layer of Case I. Fig. 1*c* shows a swollen cell containing large masses of colloid; the cytoplasm of the cell contains numerous fine melanin granules. There are a few smaller cells containing one or more colloid masses, some with, and some without pigment granules in the encircling rim of protoplasm. There are other pigmented cells,* mostly vacuolated, but without colloid contents (chromatophores, melanoblasts; see a paper read at the Lucerne Congress) both in and beneath the epithelial layer. All of these cells appear to be of essentially the same nature.

Compare with Fig. 1*c* the cell shown in Fig. 1*a*, from a section stained with ac. orceïn and polychrome methylene blue. Three small structureless spheres are seen, coloured only with the orceïn like the neighbouring colloid material, but they lie in clear spaces within the cell, differing thus decidedly from the condition in Fig. 1*c*. This cell, 1*a*, corresponds with the "Körperchenzellen," or phagocytes of lymph follicles. Fig. 1*b* shows a neighbouring similar cell, enclosing apparently a lymphocyte with nucleus darkly and uniformly coloured by methylene blue. One cannot say whether the small spheres of Fig. 1*a* are bits of colloid material that have been taken up by the cell or lymphocytes much altered by digestion.

In any case, the phagocytic cells 1*a* and *b* appear to have a different function from that of cell 1*c*, which presents no evidence of digestive action. Yet that the colloid substance in cell 1*c* has been taken up by the cell, and not formed within it, seems probable from the fairly clear distinction between colloid substance and the pigmented cytoplasm, and from the general absence of evidence of colloid degeneration within the other numerous cells present, plasma cells, etc. Here and there are scattered examples of cells such as

* The pigment is probably peculiar to dark- and yellow-skinned races, so far as colloid degeneration of the conjunctiva is concerned.

Fig. 1*d*, apparently swollen connective tissue or endothelial cells studded with clear vacuoles.

Fig. 1*e* is introduced for contrast with the above cells. It shows a plasma cell distended with hyalin refractile spheres ("Fuchsintropfen," Russell's bodies), coloured much more deeply with eosin than are the neighbouring colloid masses. There are only few such cells to be found.

The same homogeneous swelling and loss of specific staining affinities is found in colloid degeneration as in necrotic processes; and the colloid substance can perhaps scarcely be regarded as other than inert matter. In diphtheritic membrane fibrin, cells, and fibrous tissues all fuse into a uniform structureless mass containing only small refractile hyalin globules, which mostly stain with nuclear dyes. In the formation of colloid masses the evidence above given fails to indicate any very notable contributions from degenerating cells. In all of the four cases of colloid degeneration which I have seen the change was most advanced in the deeper tissues, where cells are not very plentiful.

B. Petrifaction and Ossification.

The bony spicules in Case II, found in some sections only, are in connection with a strip of fibrous tissue still remaining near the deep surface of the calcified mass; this fibrous tissue probably corresponds with the boundary of the tarsus, the colloid (and fibrous tissue) beyond being much more loosely arranged than in the main part of the mass. The mass, which, judging from the depth of colour obtained with hematoxylin, was unevenly impregnated with lime salts, is still penetrated by tracts of cells, such as those noted in Case I. Pervious blood-vessels are also fairly numerous, mostly widely dilated, with walls profoundly altered, in some cases only the endothelial lining remains, the rest of the vessel walls being merged in the surrounding homogeneous matter.

In the Trans. Oph. Soc., xxi, 1901 (q.v.), I reported a Case of Hypertrophy and Ossification of the Tarsus in a male Hindoo of 33 years.

Both upper tarsi were considerably enlarged upwards, the right one being partly ossified. In the left tarsus, which was only very moderately thickened, no abnormality was noticed in naked-eye appearance (on section) or in consistence or flexibility. The same applied to the unossified parts of the right tarsus. The apparent absence of colloid degeneration was supported by casual examination of sections of a small bit of the left tarsus excised. A recent examination, however, of these sections, and of small bits of the soft tissue attached to some of the bone removed from the right tarsus, shows unmistakable colloid degeneration, especially recognisable after re-staining with acid fuchsin and picric acid. There is homogeneous swelling of blood-vessel walls and of fibrous tissue bundles, breaking up of the latter, and fusion into blocks and masses, with loss of specific affinity for acid fuchsin. The deeper portion of the adenoid conjunctiva is also affected, but the change appears undoubtedly to have begun in the tarsus. This case is therefore closely related to the two now described, but the extensive ossification and considerable vertical enlargement of tarsus without macroscopic evidence of colloid change are extraordinary. The tests for amyloid were not applied. There was no extensive petrifaction as in Case II, reported above. The bony trabeculæ were firmly fixed in the apparently fibrous tarsus, and could not be removed without taking some of the soft tissue also.

In both the ossified cases the bony tissue is seen under the microscope to be at some points directly continuous with the neighbouring homogeneous degenerate tissue.

Description of Plates VII–VIII.

Plate VII, Fig. 1 (from Case I).—Cellular area extending deeply into tarsus. Disappearance of adenoid layer of conjunctiva to the right. Acid orceïn, polychrome meth. blue. × 120.

Fig. 2.—Much altered blood-vessel in subconjunctival tissues above the tarsus in Case II. Acid orceïn, polychrome meth. blue. × 120.

Plate VIII, Fig. 1.—Isolated cells in the adenoid layer of Case I. *a*, *b*, *c*, acid orceïn, polychrome meth. blue; *d*, *e*, hematoxylin and eosin. × 900.

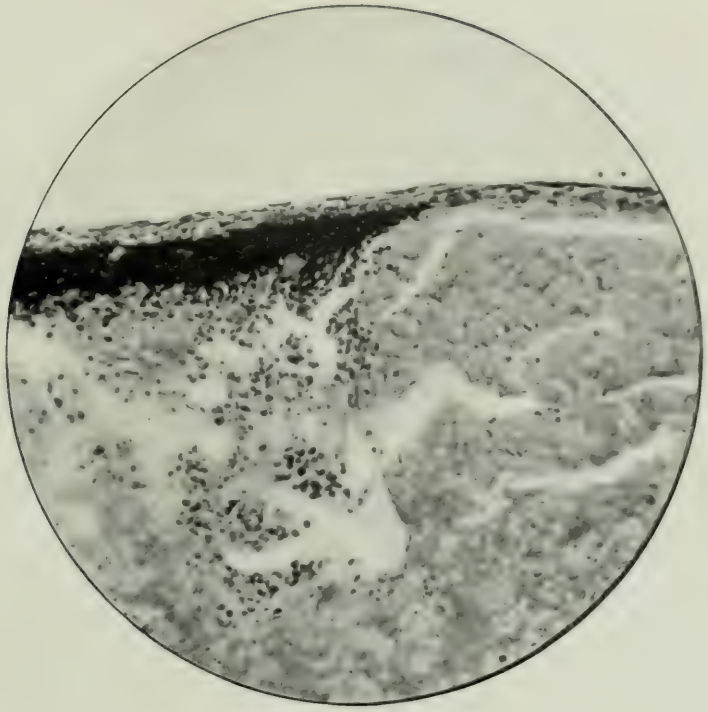

FIG. 1.

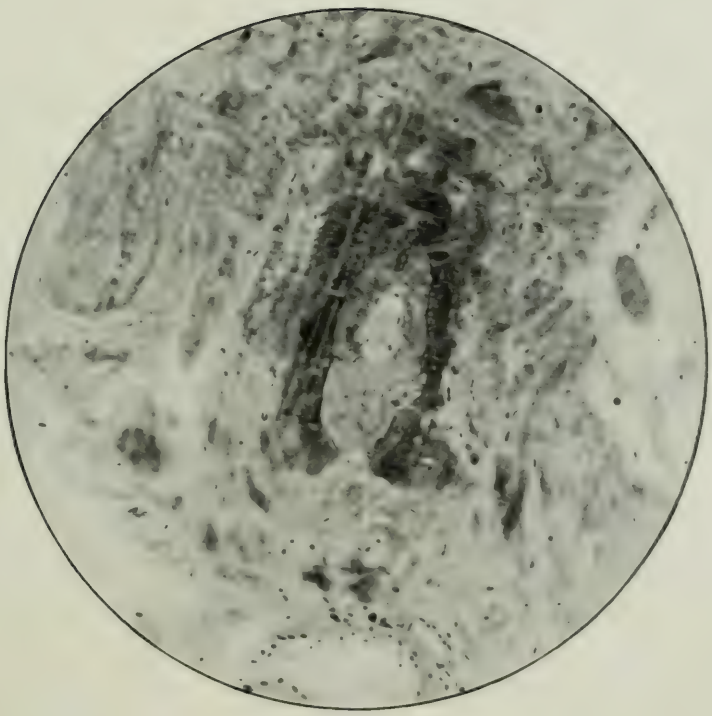

FIG. 2.

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A CASE OF GLIOMA RETINÆ IN A SHRUNKEN GLOBE.

By J. Herbert Parsons.

Edith Hopping, æt. 18 months, was admitted to the R.L.O.H. on 6.x.03, under Mr. Gunn.

The child had measles when 8 months old, pneumonia 6 weeks ago.

Family history good; 4 other children, no miscarriages; all the children have good sight.

The R. eye has been generally closed since recovery from pneumonia; it has been blind since measles. Convergent strabismus. Pain in head.

R. eye.—Globe shrunken, much injected.
Cornea hazy and infiltrated.
A.c. shallow.
Iris greenish-blue, vascular.
Lens ? opaque; fine vessels run on to capsule.
No reflex.
T –.

L. eye.—Not injected.
Cornea clear.
A.c. shallow.
Iris discoloured, vascular.
Yellowish-red reflex; vessels and hæmorrhages seen on surface.
Tn.

7.x.03. R. excision.

12.iii.04. Recurrence in R. orbit; protrusion of œdematous conjunctiva; elastic swelling felt. Child has been vomiting, and putting her hand up to the back of her head.

L. eye.—Cornea enlarged.
Iris discoloured.
Yellowish reflex behind clear lens.

6.iv.04. *R. eye.*—Contents of orbit protruding through palpebral aperture in fungating mass.
L. eye.—Marked proptosis, with fungating masses above and below.
Cornea dry and ulcerated.

8.iv.04. L. eye perforated and much more proptosed. Child very restless at night, and crying out almost continuously.

30.iv.04. Died.

Post-mortem Examination—head only examined.—Both orbits were full of gliomatous tissue, which also infiltrated and thickened the whole anterior part of the scalp and cranial bones. The chiasma was involved in a mass of growth. The roofs of the orbits were raised, so that the inferior surfaces of the frontal lobes were pitted, but not infiltrated.

Pathological Examination of the R. eye.—The R. eye was shrunken: antero-posterior diameter = 16 mm., transverse = 18 mm., vertical = 16 mm.

The eye was hardened in 10 per cent. formol, frozen, and bisected in a sagittal direction.

Macroscopic Examination.—Cornea very thick; a.c. absent; iris pushed forward; lens large, cataractous. Behind the lens is a yellowish-white mass, with reddish spots upon it; surrounding this mass is uveal pigment.

Microscopic Examination. Cornea.—Epithelium thin and ill-formed, surface level; it fills in the depressions formed by Bowman's membrane, which is very wavy. The condition very nearly resembles that depicted in my "Pathology of the Eye," vol. I, fig. 118, p. 182. Substantia propria much thickened, vascularised, and œdematous; the tissue is much spaced out, except in the anterior and posterior layers. The posterior surface of the cornea is thrown into large folds by the alteration in curvature produced by shrinking of the globe; rows of smaller sharp curves are superposed upon the large ones by wrinkling of Descemet's membrane. The endothelium is present only in places; there are microscopic deposits of pigment here and there, and some red corpuscles.

A.c.—Small and irregular.

Iris.—Transformed into a layer of fibrous tissue, with

horizontal long rod-shaped nuclei and patches of coal-black pigment scattered irregularly. It is adherent everywhere to the lens capsule.

Lens.—Cataractous. Ant. capsule thin, no cubical cells, only a few long rod-shaped nuclei. The lens substance, immediately beneath the capsule, is homogeneous. The whole of the central part of the lens is a sponge-work of broken-down fibres, granular coagula, etc. The posterior capsule is scarcely recognisable.

Ciliary Body.—Detached posteriorly; much degenerated.

Choroid (in situ).—Congested and degenerated. It is irregular in thickness, compressed in places, pulled out into a spongy mass in others. The condition is that characteristic of phthisis bulbi.

Retina.—Not recognisable, except the pigment cells. Internal to the choroid is a layer of new-formed connective tissue of irregular thickness, but greater everywhere than that of the underlying choroid. The tissue is vascular and highly cellular, the cells being spindle-shaped and asteroid, with long nuclei. It is bounded on the outer side by nearly continuous coal-black retinal pigment epithelium, which in places spreads inwards in intertwining tubules and bands.

The whole of the vitreous cavity is filled with granular material, staining with eosin. At first glance it resembles an ordinary albuminous coagulum. On minute inspection it is found to consist of degenerated cells. In a few places round nuclei, still staining with hæmatoxylin, are seen in groups, and one or two of these groups have calcareous deposits. Around the periphery there is extensive extravasation of blood.

This tissue is, I think, undoubtedly cellular, but necrotic. As far as can be made out the cells have no resemblance to leucocytes; nor are they of connective tissue origin. They do not bear much resemblance to glioma cells, but are more like the cells in the degenerated parts of gliomata than any others. They resemble the cells found in other cases of glioma in shrunken globes, some of which I have been able to compare with them.

The optic nerve is atrophic, but highly cellular. The cell nuclei vary greatly: most are oval and faintly staining, probably

neuroglial; others are rod-shaped and deeply staining, undoubtedly of connective tissue origin; others are small, round, and deeply staining, probably gliomatous, but it is impossible to be certain of this point.

Microscopical examination of portions of the orbital and intra-cranial extensions showed the typical features of glioma retinæ as it occurs in extrabulbar extensions, *i.e.*, with exuberant growth and none of the characteristic degenerative patches.

This case is of great importance as an almost incontestable case of glioma of the retina in a shrunken eye. There is only one point about the clinical history which renders causal association between the glioma and the phthisis bulbi open to doubt, viz., the fact that the blindness of the eye dates from an attack of measles at the age of 8 months, or 16 months before the child came under observation. The phthisis may have been due to shrinkage following perforation. On the other hand it is impossible to explain the peculiar degenerated cells in the vitreous on inflammatory grounds. They are indeed not characteristic of glioma, though they resemble glioma cells more than any others. Apart from the subsequent history of the case their exact nature must have remained obscure, and indeed, when I examined the eye shortly after removal, I was unable to arrive at a more definite conclusion than that the cells were probably gliomatous. In support of this diagnosis is the fact that such extensive growth of glioma in the right orbit as was discovered at the *post-mortem* examination would be unlikely from mere extension from the opposite orbit *viâ* the chiasma. Where both eyes are affected in glioma—a not inconsiderable class (about one-fourth of all the cases)—the second eye is not affected by extension *viâ* the chiasma, but is the seat of an independent growth. I have had the opportunity of examining the sections of two of the reported cases of glioma in a shrunken globe—those reported by Treacher Collins and Marshall. The cells which were regarded as gliomatous in these cases exactly resemble those

found in this case, and, as far as the nature of these cells is concerned, there is no more reason for regarding them as gliomatous in one case than in another; in no case yet reported are they absolutely typical.

I have collected from the literature 14 cases of glioma of the retina associated with shrunken globe, so that there are now 15 cases on record. The principal points of interest in these cases are briefly set out in the table appended. It is unnecessary to enter into further detail since the most important have been published in English and are readily accessible.

It will be noticed that in no less than 10 of the cases it is stated that the other eye was the seat of glioma, in another case this eye was blind, whilst in the remaining 4 the condition of the other eye is not stated, so that it may be safely concluded that it was normal. In several of the cases there is no doubt that the eye became perforated before the onset of the shrinking, usually as the result of extra-ocular extension of the growth. In the other cases it is almost impossible to decide whether perforation occurred or not; it is a difficult point to settle in a shrunken eye on pathological examination alone. There have often been inflammatory symptoms preceding the phthisis bulbi, and it is probable that the shrinking is due to this rather than to any inherent tendancy in the growth itself (Brailey), comparable with atrophic scirrhus; such an occurrence must be so rare as to almost negative the hypothesis. I am still of the opinion that the gliomatous nature of the cells in these shrunken eyes is not placed absolutely beyond cavil. It is, however, of the utmost importance that all similar cases should be carefully investigated and put on record.

There is a cognate question which is of considerable interest, viz., temporary retrogression in glioma retinæ. Such cases appear most frequently in the earliest reports, probably owing to the fact that the need for immediate operation was not recognised (Wintersteiner). Almost invariably the tumour commenced to grow again rapidly at a later date,

Case.	Author.	Sex.	Age.	Eye.	Other eye.	Duration of disease.	Clinical condition.
1	Sichel ..	?	3	R.	Glioma ..	..	Amaurotic cat's eye ..
2	Knapp ..	M.	$1\frac{3}{4}$	R.	? ..	8 days ..	Inflammation; protrusion; perforation; second perforation in 3 months; shrinking
3	Hirschberg and Happe	F.	20 weeks	R.	Glioma ..	20 weeks ..	Hyphæma; shrunken globe
4	Wadsworth	M.	14 months	L.	Blindness	8 months	Inflammation; swelling, then shrinking
5	Armaignac..	F.	26 months	R.	?	10 ,,	Shrunken globe; perforation
6	Snell ..	?	21 months	R.	Glioma ..	3 ,,	Shrunken globe .. ..
7	Brailey ..	F.	9 months	L.	,, ..	..	Painful; shrinking; hyphæma
8	Brailey ..	F.	26 months	R.	,, ..	10 months	Panophthalmitis; shrinking
9	Lawford and Collins	M.	9 months	L.	,, ..	..	Shrunken globe .. ..
10	Lawford and Collins	M.	2	L.	,, ..	..	,, ...
11	Collins ..	M.	16 months	L.	,, ..	15 months	,, ...
12	Lukowics ..	M.	18 months	L.	..	15 ,,	Varied in size; perforation
13	Marshall ..	F.	5	R.	Glioma ..	4 years 9 months	Glioma; in 3 years and 9 months shrinking
14	Lagrange ..	F.	7	L.	..	18 months	Inflammation and shrinking
15	Parsons ..	F.	18 months	R.	Glioma ..	10 ,,	Shrunken globe .. ..

Operation.	Result.	Macroscopic examination.	Microscopic examination.
Nil	Marasmus. Death ..	White tumour of retina. Optic nerve normal	Nil.
Enucleation ..	Recurrence (extirpated). Death	Red mass with hæmorrhage ..	Glioma.
,, ..	No recurrence. Death	Growth on nasal side anteriorly	,,
,, ..	Recurrence. Death ..	Filled with growth. Extra-ocular growths. Optic nerve enlarged	
,, ..	,, ,, ..	Large growth in orbit	
,, ..	Death	"Undoubtedly glioma"	
,, ..	.. ..	Thickened detached retina ..	? Glioma.
.. ..	Growth in L. and metastases.		
Enucleation ..	?	Shrunken globe; choroidal inflammation; infiltration (? inflammatory) of nerve	,,
R. eye enucleated	?	Not examined.	
Both enucleated ..	.. ..	Full of grey substance. Lens absent	"Typically gliomatous."
Exenteration ..	No recurrence in 3½ months	Globe full of tumour . ..	Glioma.
Both enucleated ..	.. ..	White mass in vitreous ..	,,
Enucleated ..	No recurrence in 2 years	Filled with growth	,,
,, ..	Death	White mass in vitreous ..	,,

and the few cases in which this did not occur may be reasonably considered to have been errors in diagnosis. The difficulties in the differential diagnosis of glioma from pseudogliomata of various kinds are often so great as to be insuperable. Many of these cases show temporary diminution of intra-ocular tension and distinct tendency to shrink, without, however, going on to complete atrophy of the globe. They, therefore, represent a group very nearly allied to the cases under discussion, and are of great importance in demonstrating that quite undoubted gliomata may show signs of shrinking at some stage of their history.

Including the cases of complete phthisis bulbi, Lagrange has collected 21 cases which showed temporary retrogression. The cases reported by Tyrrell, Rolland, Knapp and Grolmann are particularly interesting in that they showed alternate tendencies to shrink and to grow. The most striking is Grolmann's case. Here, a child of 6 had had the right eye removed for glioma 4 years previously. The left then showed a grey reflex ; no vessels could be seen. After 2 days' treatment with inunctions the mass diminished in size, and in 17 days it could only be seen with the pupil dilated. Five weeks later numerous yellow nodules were seen floating in the vitreous, and 2 months afterwards the tumour commenced to grow, accompanied by inflammatory symptoms. Hypopyon appeared, which was repeatedly evacuated, but recurred. The growth increased until it reached the lens, glaucoma setting in ; then the cornea became ectatic. Finally the tumour filled the anterior chamber, perforated the cornea, and grew rapidly outside the globe. In about a month the child died, the disease having lasted in this eye for 11 months. It will be noticed that this eye never shrank.

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A CASE OF (?) TUBERCLE OF THE RETINA.

By W. Ilbert Hancock, F.R.C.S.

A. J., æt. 19, was first seen in November, 1901, complaining of failure of vision in the right eye. The failure, gradual in onset, had extended over a period of about 8 months, but had of late increased somewhat more rapidly, which the patient attributed to an attack of mumps 6 weeks before. The youth, a farm labourer, was apparently in robust health. Careful enquiry into his family and personal history elicited nothing of importance, and Dr. Wood who kindly examined the patient reported that he could find no evidence whatever of organic disease.

Right eye, V. = counts fingers, not improved with glasses. Divergent strabismus 15°, no pain or injection. No k.p. Tn. Lens clear. Ophthalmoscopic examination showed a large yellowish-white area, situated on the temporal side of the disc and extending over the macular region (Pl. VIII, Fig. 2). The patch was roughly square in shape, the sides being equal to about 2 disc diameter, and the surface was best seen with + 5 D; the patient being emmetropic, it was, therefore, raised about $1\frac{1}{2}$ mm. Its outline was fluffy and ill defined; skirting it above and below were the superior and inferior temporal vessels respectively, the veins large and tortuous, being here and there partially obscured by retinal œdema. A few small whitish ill-defined areas were arranged immediately below and to the outer side. Two small macular arteries coursing horizontally outwards from the disc were almost at once lost to view, disappearing in the affected area. The disc, though not involved, was blurred in the temporal half and the veins were full, but there was no swelling. No hæmorrhages, new vessels, or abnormal pigmentation could be made out either on the patch itself or elsewhere in the fundus. Vitreous clear. Left eye V. = 6/6 J. 1. Fundus normal.

The patient was ordered potassium iodide and advised to return in six weeks. At the end of that time the affected area was found to have considerably increased in extent, it was then encroaching upon the nerve-head above and to the outer side. The surgeon under whose charge the patient came, recognising the gravity of the condition, the great impairment of the eye as a seeing organ, and the possibility of its being either malignant or tubercular, advised excision.

The enucleated eye-ball having been hardened in formol, frozen and bisected, was first subjected to a careful macroscopic examination. The vitreous, which was quite clear, was found to be abnormally adherent to the surface of the patch, tearing away from it with difficulty. The retina remained *in situ*, but on subsequently passing the eye through spirit it became detached, and it was at once seen that the morbid focus was entirely confined to the retina, the choroid and overlying pigment epithelial layer both to the naked eye and examination with the corneal loupe appearing quite normal. After embedding, colloidin sections were cut, which showed the following characteristics:—

The retina is thrown into numerous folds and separated from the choroid by a narrow band of exudation staining deeply with eosin (Pl. IX). The choroid is normal in appearance, the membrane of Bruch intact and covered by an apparently unaltered layer of hexagonal pigment epithelium. In the thickened folded retina are two well-defined plaques of granulation tissue; these in the majority of the sections are seen to be quite distinctly separated from one another by retinal layers which, though quite recognisable, have undergone more or less change, but in a few sections they are seen to be connected by a band of fibrous tissue which, as it were, perforates the intervening retinal layers (Pl. X, Fig. 1). The anterior or internal plaque, confined to the nerve fibre layer, is chiefly composed of ill-developed fibrous tissue containing well-marked giant cells, and exhibits extensive round celled infiltration (Pl. X, Fig. 2). The giant cells are of the large branching type with well-defined nuclei

arranged without exception in the centre of the cell. The small celled infiltration is especially evident in the perivascular lymph spaces and bears no definite relation to the giant cells, nor are the latter surrounded by any epithelioid cells as in typical tubercular systems.

The posterior or external plaque, confined, to the rod and cone and external nuclear layers, is also chiefly made up of cellular fibrous tissue, but differs markedly from the anterior in containing a large number of blood vessels and proliferated pigment epithelium, and there is an entire absence of giant cells. The whole affected area is sharply limited, passing abruptly into œdematous but otherwise normal retinal tissue. No tubercle bacilli could be demonstrated. Whether the anterior or the posterior plaque was the primary seat of the lesion it seems impossible to determine. The cornea, iris, lens, ciliary body and optic nerve were normal.

The above sections show that we are obviously dealing with some chronic inflammatory change in the retina, and the question arises as to its causation. Syphilis may, I think, be definitely excluded, there being no evidence of the inherited or acquired form of the disease, and the patient denied most emphatically ever having exposed himself to infection. This being so, one naturally asks is it tubercular? The patient's family history throws no light on the subject. His father died at the age of 76, of senile decay; his mother is alive and well, and his only sister enjoys excellent health. There have been no other children, and as far as could be ascertained, there is no history of tubercular disease either on the paternal or maternal side of the family. We have, therefore, to form an opinion on the histological characteristics alone.

The presence of giant cells in the anterior plaque would lend weight to the tubercular origin of the growth, but at the same time it must be admitted that the character of these cells is not that generally associated with tubercle nor, as mentioned above, is there any sign of tubercular systems. On the other hand, it is generally recognised that the

FIG. 1.

FIG. 2.

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FIG. 1.

FIG. 2.

Bale, Sons and Danielsson, Ltd.

histological characteristics of tubercular lesions are extremely variable, and that there are but two ways of positively asserting a lesion to be of that nature. Firstly by inoculation experiments, which were obviously impossible in this particular case. Secondly, by the demonstration of the specific organism. This latter is a purely positive test and the eye-ball having been hardened in formol would render the demonstration of the tubercle bacilli, even if present, extremely uncertain. It seems, therefore, reasonable to look upon the case as one of retinal tuberculosis, until further information on this class of case is forthcoming.

The case is also interesting in that it is an example of a not uncommon class met with clinically, that of the large solitary patch of inflammation situated, as a rule, in the vicinity of the disc, especially in the macular region, and which we have so seldom an opportunity of examining microscopically.

Careful search through ophthalmic literature has resulted in my finding several references to the subject of retinal tuberculosis. O'Sullivan and Story publish an extremely interesting case of the condition, confined to the internal retinal layers and commencing in the immediate vicinity of the disc. This seems to be the first recorded case of the disease which has been diagnosed clinically, and subsequently verified by microscopic examination. In this case there was no evidence of tuberculosis in any other part of the body, but as the authors rightly point out, it is of course difficult to exclude this possibility.

Ginsberg speaks of it as being invariably secondary to tubercle of some other part of the eye, *e.g.*, iris, ciliary body, or choroid, and indeed it is not uncommon, especially in the latter condition, to find isolated foci of the disease in the retina. Tubercle of the optic nerve with or without implication of the retina, has been described in a few cases, notably by Bongartz, Demours, Cruveilhier, Wagenmann and Sattler, but in all these cases there was evidence of a similar disease in some other part of the body.

Schöbl, Bach, Perls and Manfredi, all speak of retinal tuberculosis, but these cases are obviously secondary to implication of some part of the uveal tract.

In conclusion my best thanks are due to Mr. Richardson Cross for his kind permission to publish the case, and also to Mr. W. T. Lister for the admirable micro-photographs which serve to illustrate this paper.

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Description of Plates VIII–X.

Plate VIII, Fig. 2.—From a rough pencil sketch of the fundus made on the patient's first visit to show the position and extent of the affected area.

Plate IX.—Section showing the folding of the retina and the anterior and posterior plaques separated from one another by easily traceable retinal layers.

Plate X, Fig. 1.—Section of retina showing the anterior and posterior plaques connected by a fibrous strand which perforates the intervening retinal layers.

Fig. 2.—The anterior plaque of the section in Pl. IX, under a high power, showing the giant cells and small cell infiltration.

INTRADURAL TUMOUR OF THE OPTIC NERVE. NEURO-FIBROMATOSIS.

By M. S. Mayou.

(From the Andrew Clark Laboratories, London Hospital.)

Intradural tumours of the optic nerve are not common, although not exactly rare.

F. Lagrange[1] has collected some 173 cases: Byers,[2] 102 cases; Lawson,[3] Treacher Collins, Marshall[4] and Werner[5] have published some cases in this country, Lagrange, Byers, and Werner having reviewed the subject as a whole.

The object, therefore, of describing this case is that the tumour was removed when comparatively small, and it shows well the distribution of the nerve fibres and the origin of the tumour.

L.J., female, æt. 5, attended Moorfields on March 9th, 1904, complaining of right convergent strabismus. At the same time it was noted that the right eye was apparently smaller than the left, which was probably due in reality to a slight proptosis in the left eye. Her refraction was estimated by retinoscopy, and was

Rt.	Lt.
+3 / +3	+6 / +6

On July 25th, 1904, the patient came under my observation at the London Hospital whilst I was doing Mr. Lister's work.

There was a history of slowly increasing proptosis, noticed first in December, 1903, with loss of vision in the left eye. There was no pain, and otherwise the child seemed a strong healthy girl, apart from some adenoids with secondary deafness.

The proptosis was not great in amount and the lids could be easily closed over the globe. The eye was pushed straight forward.

The movements of the globe were not limited.

No tumour could be felt, no pulsation or bruit distinguished.

The globe was not congested. The pupil was inactive to light but reacted consensually.

Media, clear.

The fundus showed well-marked optic atrophy. The edges of the disc were somewhat blurred and a small amount of exudation could be seen along the vessels.

The arteries were small but the veins were considerably enlarged.

V.L. no P of L.

By retinoscopy I estimated the refraction as $-\left|\frac{+7{\cdot}5}{+7{\cdot}5}\right.$ in the left eye; that is to say, there had been an increase in the hypermetropia. On this point the gentleman who performed the original retinoscopy did not agree.

On July 28th, 1904, a vertical incision was made along the outer wall of the orbit to the bone. The periosteum was then stripped up from the inner surface of the orbit and incised. On passing the finger behind the globe a hard rounded tumour could be felt, wedged into the apex of the orbit. Horizontal incisions were carried outwards from the upper and lower end of the original incision, reaching down to the bone. The outer bony wall of the orbit was then sawn through above and below into the spheno-maxillary fissure, and the flap together with the bone turned outwards. Although this gave ready access to the tumour the posterior part of it could not be seen. There was at least $\frac{1}{2}$ cm. of free nerve between the globe and the tumour. Keeping as close to the tumour as possible a pair of curved scissors were passed behind the tumour from the outer side and the nerve divided as close to the optic foramen as possible. It was then freed in front by dividing the nerve close to the globe. The flap was replaced and sutured in position by skin stitches. No drain was put in the wound. The wound healed by first intention and the sutures were removed on the 4th day. Some trouble was given by the enormous proptosis which was present for some days after the operation, and indeed a small ulcer formed on the lower part of the cornea, which subsequently healed.

On August 24th the patient was discharged from the hospital.

At that time there was complete ptosis although the lid could be slightly raised. The cornea was anæsthetic and the movements of the globe were nil. The fundus was difficult to make out as there was some opacity in the media. It was pale, but the vessels could still be seen.

On October 26th the eyelids could be raised to a slight extent. The vessels of the bulbar conjunctiva were dilated. The globe showed some movement and there was slight enophthalmos; the pupil was widely dilated, and there was some return of sensation to the bulbar conjunctiva. The cornea was hazy below, owing to the pressure of the lid margins and the nebula left by the old ulcer.* The pupil did not react consensually.

Fundus.—The area of the disc was occupied by a mass of white exudation which protruded forwards to a slight extent into the vitreous, the exudation extending into the retina along the vessels. At the edges of the upper part of the mass of exudation the retinal vessels could be recognised, especially the veins, which were very full. These vessels contained blood, but it was impossible to determine the direction of the blood-stream in them. Further out, beyond the exudation, there was some disturbance in the choroidal pigment.

Morbid Anatomy.—The tumour measured 2·5 cm. long and 1·8 vertically. It was fusiform in shape, the diameter of the optic nerve at the cranial end measuring double that in front of the tumour. It was situated entirely within the dural sheath. Spread out over the surface and more or less incorporated with it were the long ciliary nerves together with the ophthalmic artery. Near its posterior part was a small portion of a nerve of larger calibre which was probably a portion of the third nerve. As the tumour was jammed into the apex of the orbit the cutting of these was unavoidable. The tumour was hardened in formol for 24 hours and divided longitudinally. On section it was white in colour and not very vascular. The central artery of the retina was present in it and there was some softening and hæmorrhage near its centre. Portions of the tumour were embedded in paraffin and subsequently stained with logwood and

* Since this date a small trophic ulcer has formed in this situation.

eosin; others were put into Muller and Muller and osmic acid and preparations made by Marchi's and by Weigert's methods.

Microscopic sections showed that the tumour was completely encapsuled by the sheath of the dura mater, which was not infiltrated by the tumour. In front of the tumour this sheath was considerably distended, and this, with the pressure of the tumour on the central vein, no doubt accounted for the optic neuritis which had been present. The tumour consisted of two portions: the lower, through which the optic nerve ran, and the upper, which did not contain any part of the optic nerve. Separating these two was a fine membrane which seemed to be derived from the pial sheath, through which I think the upper part of the tumour had spread. The upper part of the tumour consisted of cells of the type found in the trabecula of the optic nerve and enclosing spaces which I think were attempts at reproduction of the spaces found in that structure for the nerve bundles. All these spaces were very irregularly arranged. In the lower part of the tumour where the nerve was present there were no spaces, the increase of interstitial tissue being arranged longitudinally between the nerve fibres, each individual nerve fibre being widely separated from any other. Where the nerve was cut through posteriorly the interstitial tissue was considerably increased, although there were no irregularly arranged spaces as seen in the upper part of the tumour, there being simply a general increase in the neurilemma. The optic nerve close to the globe was free from any increase in interstitial tissue and was of about its usual calibre, the fibres staining well by Weigert's method. As the nerve passed backwards the fibres showed by their absence most degenerative changes in two situations:—

(*a*) In the upper part of the nerve, just before entering the tumour; that is to say, at the point where kinking of the nerve took place by the movement of the globe in front of the tumour.

(*b*) In the upper part of the nerve, within the tumour, at the point of its greatest diameter, where most separation of the nerve fibres had taken place.

The nerve fibres themselves showed very marked beading and wavy outline, partly, no doubt, due to degeneration, but partly due

to technique, as the tumour was not pinned out while being hardened. In some situations actual rupture of the nerve fibres seems to have taken place. Although Marchi's method was followed with every care, on two separate portions of the tumour no staining of the myelin sheath could be made out. This, perhaps, is accounted for, since the tumour must have existed at least 7 months, and therefore the destruction have been very slow and the material staining by Marchi's method absorbed.* No axis cylinders could be made out in the logwood and eosin sections.

The cytoplasm of the cells was very ill defined. The nuclei are of two types; one the large oval elongated faintly staining nucleus resembling those of endothelial cells, and the second a small rounded darkly staining nucleus. The cells are not undergoing mitosis to any extent; only one cell in the aster stage could be found in section after examining under a $\frac{1}{12}$th for an hour. The type of mitosis in this cell could not be made out.

The blood vessels in the tumour were extremely scanty, but where present were well formed and usually had both endothelial and perithelial coverings.

Conclusions.

The *Etiology* of this case, taking Byers' statistics, is very typical.

The *age* was 5 years. Six-eighths of the cases appear before the age of 15 and five-eighths before the age of 10.

Sex.—The patient was a girl. The female sex provides 59 per cent. of the recorded cases.

Side.—The left side is more frequently affected than the right, 55 per cent. It was the left side which was affected in this patient.

Symptoms and Clinical Appearance.—Failing vision with a painless proptosis, the eye being pushed straight forward with very little limitation of movement; secondary optic

* Degeneration changes have not been shown to occur in neuro-fibromata of the spinal nerves, although motor paralysis has been recorded (A. Thompson[6])

atrophy with distended veins, and increasing hypermetropia are all cardinal signs which were present in this case.

Pathological Anatomy.—The condition was one of neuro-fibromatosis of the optic nerve. The irregular fusiform shape of these tumours seems fairly constant and, as in this case, usually affects the part of the optic nerve at the back of the orbit. It is extremely probable that the diffuse enlargement of the nerve extended within the skull as there was a great increase of interstitial tissue which extended right up to the optic foramen, although in this situation there was no overgrowth outside the nerve proper. That this thickening does occur within the skull has been shown by Byers in 11 cases which he has collected, all of which, with the exception of 2, died from meningitis after operation. One of the others died of pulmonary tuberculosis, and in one of Byers' own cases death was due to the actual growth of the tumour within the skull.

The localised swelling, which was external to the nerve proper, was identical in structure with the nerve sheath, the spaces found in it being attempts at the reproduction of the spaces for the nerve bundles, the condition, therefore, being a general increase of interstitial tissue with a localised overgrowth outside the nerve. Presumably owing to the presence of these spaces some of these tumours have been called lymph-angiectasis fibroma, but, as has already been pointed out, these spaces are not lined by endothelium but are lined by the actual cells of the tumour. It is probable that most of the recorded cases belong to this type, the great variety of names which have been given to them being due to secondary degenerative changes in the tumour. Thus myxo-fibroma has been applied to those cases in which the spaces have become distended with a homogeneous coagulum.

Although it is probable that myxo-sarcomata do occur, many of these tumours have been described as malignant on insufficient data: namely, the occurence of other tumours along the course of the same or other nerves; unless there is infiltration of the orbital tissue with the growth, or

secondary growths apart from nerve tissue occur, or unless possibly the type of mytosis in the cells can be demonstrated, it is not correct to call these tumours malignant. Endotheliomata undoubtedly occur within the nerve sheath but form an entirely different type of tumour from the neuro-fibromata.

The destruction of the nerve fibres in my case was most evident in two situations:—

(*a*) In the central part of the tumour; that is to say where the pressure is greatest, and

(*b*) At the point where the nerve passes into the tumour in front; especially is this evident in the upper part of the nerve. This seems to be undoubtedly due to the kinking of the nerve at its junction with the swelling.

It is probable that some destruction of nerve fibres is also produced by the fibrosis following the optic neuritis, although there was not much evidence of this, as these myelin sheaths directly behind the disc took up the stain readily. The destruction of the fibres seems to be comparatively slow, since staining by Marchi's method showed no changes in the myelin sheath; probably this was due to the absorption of the material staining by this method.

The cause of the optic neuritis is obviously due to the distension of the nerve sheath between the tumour and the globe, probably secondary to pressure on the central vein which was involved in the tumour and was engorged both within (ophthalmoscope), and behind the globe. The secondary optic atrophy is more difficult to explain, the chief factors in its production being fibrosis together with the dilatation of the communicating veins between the central vein and the veins of the nerve sheath.

The regurgitation of blood into the retinal and choroidal vessels after division of both the main ophthalmic artery and the central artery is of considerable interest; unfortunately owing to the condition of the media the earliest stages could

not be observed, but, as has been shown by Knapp[7] and Parsons[8], after division of the central vessels the distal end becomes occluded and blood finds its way back into the vessels from the perforating branches of the anterior ciliary vessels. The ophthalmic artery in this case was divided near the foramen; although it is possible that some muscular branches may have escaped, the conjunctival congestion which persisted was suggestive that in this case an additional source of supply was the anastamosis between the anterior ciliary and the posterior conjunctival vessels and so back to the perforating arteries.

The return of sensation to the conjunctiva and of the motor power to the muscles were probably dependent on the regeneration of the nerves, the exact method of which is as yet to be demonstrated.

In conclusion I have to thank Mr. Herbert Parsons for the use of the hospital camera and for the assistance he has given me in taking the microphotographs which illustrate this paper.

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Description of Plates XI–XIV.

Plate XI, Fig. 1.—Full face view of L. J., showing proptosis of the left eye.

Fig. 2.—Tumour after removal, showing the ciliary nerves and ophthalmic artery adherent to the capsule.

Plate XII, Fig. 1.—Longitudinal section of the tumour (Weigert, Pal.). Note the lower part of the tumour contains nerve fibres; also the difference in size of the nerve anteriorly and posteriorly. There has been some hæmorrhage near the centre of the tumour.

FIG. 1.

FIG. 2.

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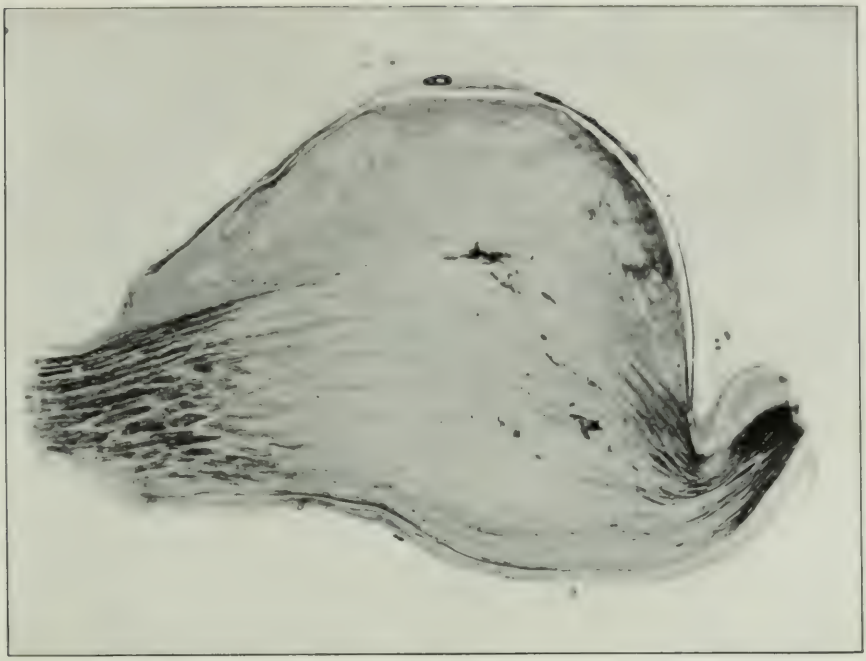

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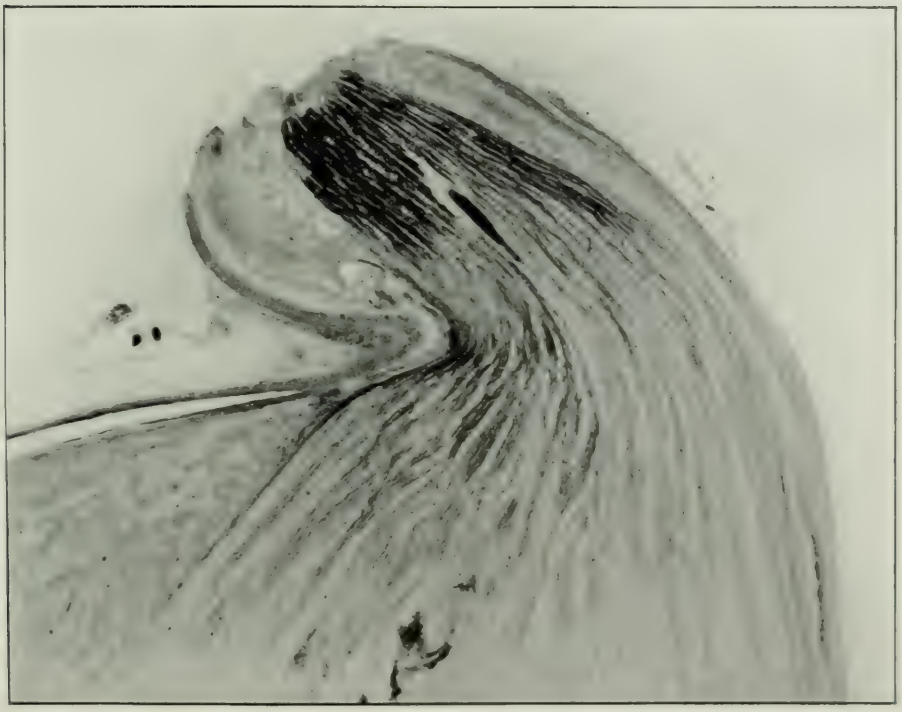

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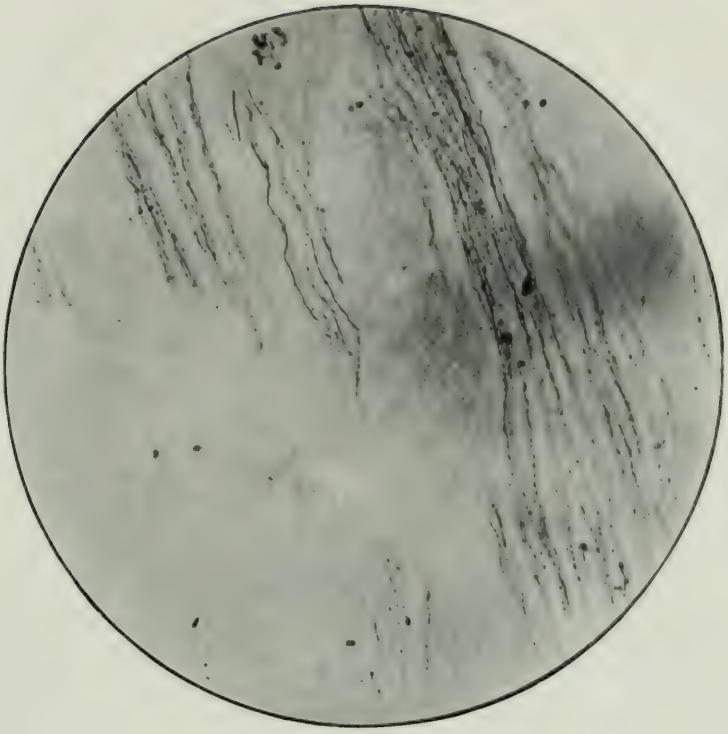

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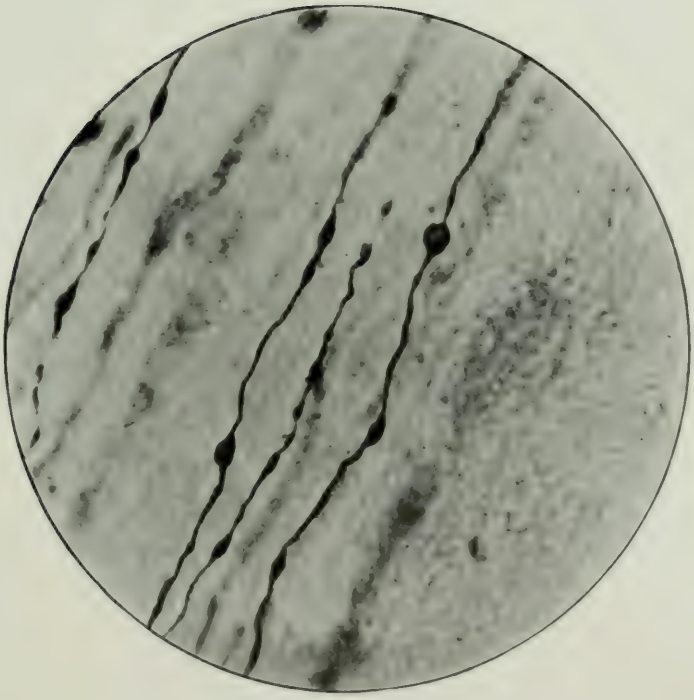

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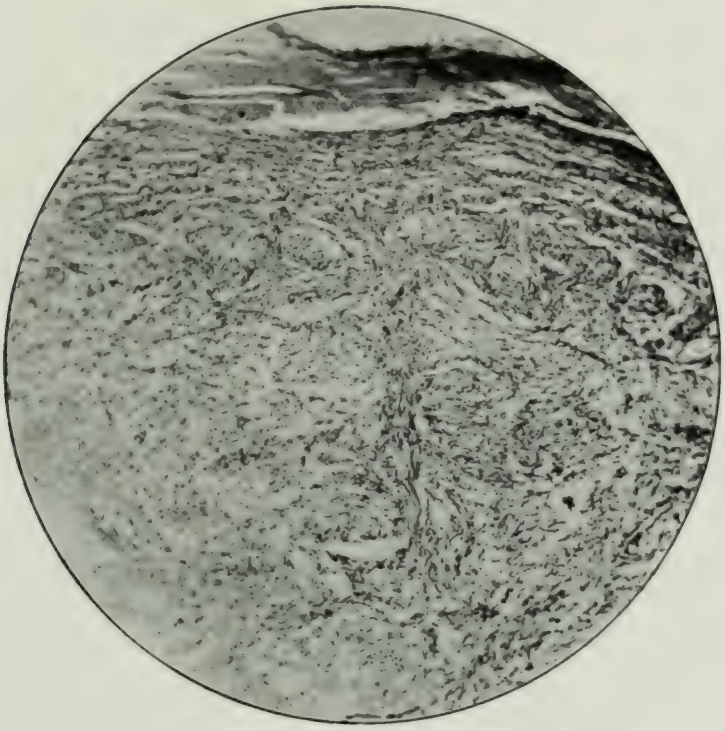

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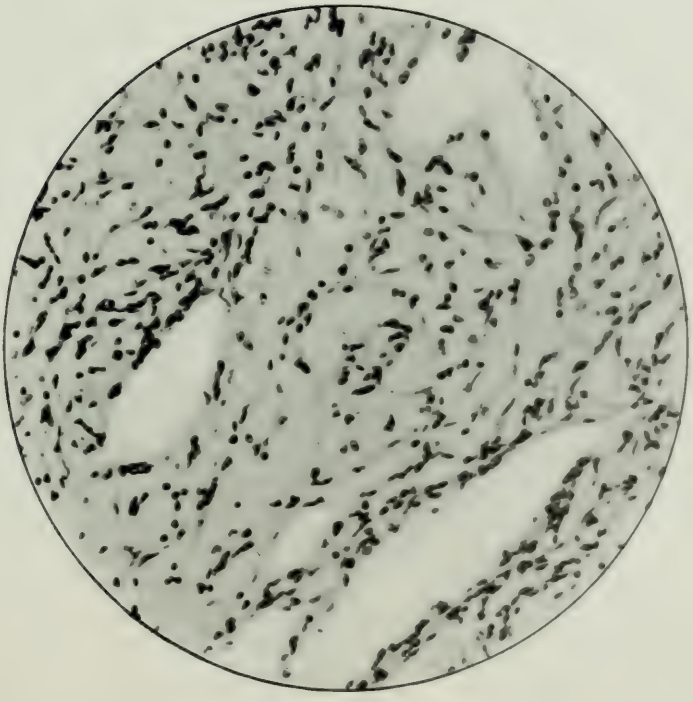

FIG. 2.

Bale, Sons and Danielsson, Ltd.

Plate XII, Fig. 2.—The anterior end of the nerve and tumour (Weigert—Pal.). Note (*a*) the distension of the nerve sheath in front of the tumour; (*b*) the degeneration in the upper part of the nerve produced by the kinking; (*c*) the process of the pial sheath passing between the upper and lower portions of the tumour; (*d*) the separation of the nerve bundles by interstitial tissue.

Plate XIII, Figs. 1 and 2.—Showing the separation of the nerve fibres by interstitial tissue (Weigert—Pal.). Fig. 1 also shows a nerve bundle which has probably ruptured. Fig. 2, beading of the nerve fibres.

Plate XIV, Fig. 1.—Upper portion of the growth, showing the trabecula spaces. In the upper part of the section can be seen the dural and arachnoid sheath. (Logwood and eosin.)

Fig. 2.—High-power view of the same. Note the spaces are lined by the cells of the tumour. (Logwood and eosin.)

THE STRUCTURE OF THE MEMBRANE OF BRUCH, AND ITS RELATION TO THE FORMATION OF COLLOID EXCRESCENCES.

By GEORGE COATS.

(From the Pathological Laboratory.)

THE histological details of "colloid excrescences" of the membrane of Bruch have been tolerably fully worked out. We know that they appear first as small homogeneous or slightly granular bodies underneath the pigment epithelium in close connection with the membrane of Bruch, and that they grow either singly or by coalescence in the form of little nodular masses. Only when they have reached some size do they lose their homogeneous structure and undergo various secondary changes, *e.g.*, lamination, disintegration of their centres, calcification, formation of a central core of connective tissue (probably by invasion), and, finally, bone formation from ossification of the invading connective tissue. So much is well known and universally admitted; when, however, we come to the explanation of the origin of these bodies, we meet with considerable diversity of opinion, in spite of the very large amount of work which has been done on the subject.

Certain theories may be put aside as discredited or inherently improbable, such as Rudnew's, that they arise from hyaline degeneration of wandering leucocytes, and Pes's, that they may arise by processes of sclerosis and atrophy in superficial papillæ of the choroid formed in consequence of the cicatricial contraction following upon inflammation in the middle and deep layers of that tunic. The theory of Hofmann also may be merely mentioned; this author states that they arise from hyaline degeneration of thrombi in the choriocapillaris vessels, or of the endothelial cells lining their walls. The hyaline masses so

formed project in their growth against the membrane of Bruch, and finally rupture it and pass through to the inner side, after which, so says Hofmann, the membrane heals up again, and thus is produced an appearance as if the membrane of Bruch ran past the excrescence unchanged. This appearance undoubtedly occurs (see Pl. XV, Fig. 4), and has been the cause of much of the controversy, since it has led many to deny to the bodies any connection histologically or developmentally with the membrane of Bruch. I shall discuss the point later.*

No one who has examined many of these excrescences will be inclined to consider these three theories when he notes how strictly the bodies are confined to the inner layers, and how they not infrequently occur in choroids quite free from all traces of inflammation, past or present. Leaving these explanations, therefore, out of consideration, opinions will be found to be divided into two main camps: (1) The excrescences arise from actual transformation of the cells of the pigment epithelium. (2) They arise, as the membrane itself is supposed to arise, as a deposit from the cells of the pigment epithelium, but without actual transformation of pigment cell into excrescence. The former of these may be conveniently referred to as the "transformation" theory, the latter as the "deposition" theory.

The transformation theory, which was first enunciated by Donders, has, perhaps, the most supporters, and seems to be favoured by recent investigators, at least in Germany.† The details of the process are variously given by different authors. Donders believed that the nucleus became hyaloid, and so formed a minute excrescence, but it was afterwards pointed out (by de Vicentiis) that it was more consonant with general pathological principles that the protoplasm

* It should be stated that Hofmann, arguing from this supposed origin, believes that the bodies described by him are not ordinary colloid excrescences, but neither in his description nor in his figures can any warrant be found for placing them in any other class.

† An historical review, with references to literature, will be found at the end of this paper.

should be first affected by a degenerative process. Since the colloid bodies were found mostly in the eyes of old people, it was natural to connect them in origin with the well-known senile changes in the epithelium. It was, therefore, explained that the pigment epithelium became irregular in its arrangement, some of the cells being larger than others and sometimes containing two nuclei; the layer might also be doubled. In addition the pigment was irregularly distributed, denser in some places and thinner in others, while the little rods normally found were replaced by round granules. Certain of these pale cells became more and more homogeneous, lost their nuclear staining, and finally became converted into small colloid bodies which grew by accretion. Or, according to others (*e.g.*, Dimmer), colloid globules appeared within the cell-protoplasm which, becoming larger by confluence, finally destroyed the cell and formed a minute colloid body, the larger being the result of the fusion of many smaller.

There are many difficulties in accepting this theory of origin. In the first place the histological appearances do not support it, for in an early stage the bodies, if stained in the usual manner with eosin, have the appearance of being thickenings of the membrane itself, provided that the section passes through their middle (see Fig. 3). They seem, however, early to form a knob-like head, and if this is cut peripherally, the nodule will naturally seem to have no connection with the membrane of Bruch. Again, while it is true that the pigment epithelium in many cases shows alterations, these have no constant relation in distribution to the colloid bodies, as has been shown by Kerschbaumer, and are to be regarded like the colloid bodies themselves as pathological, or in some cases as senile changes. The proof of cause and effect, therefore, is inadequate, and definite transitional forms have not been sufficiently clearly described and figured. Another very serious difficulty consists in the fact that the bodies, even when of large size, remain covered with epithelium, often flattened and depig-

mented, but seldom broken through (Pl. XVI, Fig. 1). Why should this be so if they arise from one or several pigment cells? Would the swelling cell not rather push its neighbours aside and remain uncovered? The explanation has been put forward that adjacent cells grow over, but why should they do so, and if they did, why should they form in so many instances a single uniform layer? It is surely more likely that the excrescences have a uniform covering, because they originated underneath the epithelium and merely raised it up. Over small nodules the epithelium will often be found to all appearance quite unaltered. Another explanation, still more unlikely, is that only part of the cell becomes involved in the degeneration, while the nucleus and unaffected part of the protoplasm form the well-stained lining. But this is surely supposing a thing very unlikely in the life history of an individual cell, nor are the cells firmly adherent to the excrescences as they ought to be if the latter were formed from part of their protoplasm.

Again, the size to which single nodules may grow (Pl. XVI, Fig. 1) is against their origin from one cell and strongly in favour of an origin by deposition or secretion; no case of a cell expanding to so great a size can, I believe, be produced in pathology. The remark does not, of course, apply to tuberculated or compound nodules such as are often found, since these might arise from the fusion of many cells. Nor does this exhaust the indictment against direct transformation; in the earliest stages the excrescences never separate with the pigment epithelium, but always remain firmly attached to the membrane of Bruch, although it is said that when large and standing upon a thin pedicle, they may break off and even be found in the outer layers of the retina. Again, Donders himself has shown that they react in all respects to reagents like the membrane itself, being highly resistant to water, alcohol, ether, acids, alkalies, mechanical injuries, etc., and failing, like the membrane itself, to take on the stain for amyloid substance.

A chain of arguments is thus raised against an origin

by direct transformation, each link of which seems to furnish proof for the second theory—that the excrescences are formed by deposit from the cells of the pigment epithelium in the same manner as in all probability the membrane itself was formed. The case in favour of this hypothesis, which was first stated by Heinrich Müller, may be put thus: In an early stage the bodies appear histologically to be simple localised bulgings inward of the membrane; they show no constant relation in localisation to those changes in the pigment epithelium, found in old and diseased eyes, which have been described as intermediate in the process of transformation; single nodules may grow to a large size while still remaining covered with a well-marked unicellular layer of epithelium; they do not separate with the epithelium when the latter strips off; they react to chemical, mechanical, and staining agents in all respects like the true membrane. In addition the analogy of the outgrowths of the membrane of Descemet may be cited. These also show no appearance of arising by transformation of the endothelial cells, but present themselves as localised inward bulgings of the membrane itself, lined by a well-preserved single-layered endothelium. In the case of the membrane of Descemet also, the proof is very complete that the endothelial cells are capable of laying down homogeneous substance, witness the membranes which sometimes form on the front of the iris in cases of anterior synechiæ (see Wagenmann, etc.).* The case of the capsule of the lens furnishes, perhaps, an even more complete analogy, since, like the membrane of Bruch, it is lined by epithelial cells of epiblastic origin, and Mr. Collins has shown that these cells also are capable of laying down new homogeneous substance.†

How then are we to explain the statement so often and

* Wagenmann, Arch. f. Ophth., 1892, vol. xxxviii, pt. 2, p. 91; Müller, Arch. f. Ophth., 1856, vol. ii, pt. 2, p. 48.

† Collins, Trans. Ophth. Soc., 1892, p. 89 (fig. at p. 100). See also Leber, Sitzungsb. d. Ophth. Gesellsch. z. Heidelb., 1878, p. 33.

so definitely made by supporters of the transformation theory that the membrane of Bruch can be seen to run past colloid bodies and to take no part in their formation? If it can really be shown to be so, then in spite of the arguments adduced above to show that they *ought* to arise from that membrane, we must either admit ignorance or find some new mode of origin for them. Nor can the statement be dismissed as founded upon a mere error of observation. There *is* such an appearance, as may be very clearly seen in Fig. 4, Pl. XV, and Fig. 1, Pl. XVI. Allusion has already been made to the fact that this would be produced if the nodule had a slender pedicle and a large expanded head, and if the periphery of this head were cut by the section, but not the pedicle. This, no doubt, is the explanation in some cases, but not in all, for it is a matter of experience that small excrescences, at least, are sessile, yet even in these the membrane of Bruch seems to go past unaltered (Pl. XV, Fig. 4). There is, however, another and most important factor in the structure of the membrane itself, a factor which seems to furnish the solution of the problem. In sections of ordinary thickness, prepared and stained in the usual manner, this membrane appears homogeneous or slightly granular (Pl. XV, Fig. 1). Yet even in early descriptions (Sattler, etc.), a finely reticular appearance of the outer aspect, and a tendency to split into two layers on macerating with strong salt solution were noted. Recently the key to this appearance has been given by methods of special staining. The reticular appearance is, in fact, due to a layer of very fine elastic fibres. In specimens stained with Weigert's elastic tissue stain, this is very plainly brought out (Pl. XV, Fig. 2). The separation into two layers is most distinct in the neighbourhood of the papilla where the membrane of Bruch is thickest, and the distinction is further emphasised here by the fact that the two portions end differently. The inner homogeneous portion, next the pigment epithelium, ends with the ending of the pigment epithelium, a further proof that it is a product of these cells. The outer elastic portion, which

can easily be seen with high magnification to be composed of a feltwork of exceedingly fine sharply stained elastic fibres, goes on into the substance of the papilla for some little distance, and finally terminates with a curious curly upturned end (Pl. XV, Fig. 2). It may be remarked in passing that Weigert's elastic tissue stain is specific only for elastic fibres and the elastica interna of vessels. A certain diffuse blue staining of a membrane, usually regarded as "elastic," is no proof that it contains the same substance as the true elastic fibres and membrane of Henle. For instance, the membrane of Descemet, the zonula, the lens capsule, the dilatator iridis, the sphincter pupillæ, and the homogeneous portion of the membrane of Bruch, all stain diffusely, but do not take on the intense blue staining which is characteristic of true elastic tissue.*

A further proof of the composite nature of the membrane of Bruch is furnished by its method of terminating towards the ciliary body. About the level where the pars plana gives place to the pars ciliaris retinæ the outer elastic layer becomes looser in texture, and being joined by elastic fibres from the general choroidal stroma, forms a meshwork of fine fibres. Through the openings of this meshwork connective tissue with a few fine vessels becomes insinuated, so that it no longer lies immediately underneath the pigment epithelium but is separated from it by a little distance. Tracing the fibres forwards they do not enter into the ciliary processes, but run straight on past their bases in the fine connective tissue between the ciliary muscle and the ciliary processes. Finally they end near the root of the iris not far from the elastic fibres given

* There is, however, some reason to suppose that the membrane of Descemet contains true elastic substance. It stains more deeply than the other membranes mentioned here, and fine elastic fibres may be seen passing off into the scleral tissues from its termination. There is, moreover, some evidence that the membrane of Descemet, like the membrane of Bruch, is composite in structure. It also has a tendency to split longitudinally, and in the case of colloid excrescences from it, an anterior layer may sometimes be seen to pass on unaltered, while a posterior layer bulges out to form the excrescence (see a picture in Wagenmann's paper, mentioned on p. 168).

off from the ligamentum pectinatum, but without coming into direct contact with these. The inner homogeneous part of the membrane, on the other hand, is described as entering into and following the sinuosities of the ciliary processes, forming in fact, a basement membrane for the pigment epithelium. Even in the anterior part of the true choroid, however, the homogeneous membrane is very thin, and in the ciliary processes it becomes difficult even in depigmented specimens to be sure that any definite membrane occurs. Rather the epithelium seems to rest directly on wavy connective tissue bundles, with at most the intervention of a linear basement membrane. There is at least in the ciliary processes no membrane staining specifically with Weigert's elastic tissue stain, and, indeed, except for an occasional isolated fibre usually accompanying a vessel, no elastic tissue in them at all.

The above details have been given in order to show that the membrane of Bruch which seems homogeneous when stained with eosin (Pl. XV, Fig. 1), can be resolved into two layers by special staining (Pl. XV, Fig. 2). It seems highly probable that the difference represents a difference in origin. The fine elastic fibres of the outer layer are in all respects similar to the elastic fibres found in the neighbouring choroid, and must, therefore, be looked upon as contributed by the choroid, since it is impossible to believe that definite elastic *fibres* could be laid down by the epiblastic pigment epithelium. The inner homogeneous layer on the other hand has all the appearance of a cuticular product laid down by the epithelium in the same manner as the lens capsule is laid down by its epithelium. The probability is, therefore, strong that it has been contributed by the pigment epithelium. It may be said that only the inner homogeneous layer ought to be reckoned as the membrane of Bruch (or lamina *vitrea*), and no doubt this would be convenient, but the present point is that the "membrane of Bruch" as seen in sections stained in the usual way includes both layers.*

* Or, on the other hand, it might be argued that the name should be used for the outer elastic layer, which would allow us to retain the synonym.

Applying now these observations to the elucidation of the origin of colloid bodies, it will be found that there is much evidence in favour of the view that they arise from the inner homogeneous layer and from it alone. The argument would run somewhat as follows. The homogeneous portion of the membrane of Bruch is a cuticular product from the pigment epithelium, and in a similar manner under the influence of certain pathological stimuli, these cells may lay down irregular nodules of the same substance. On the other hand, the elastic portion is a mesoblastic product belonging in reality to the connective tissue of the choroid, and takes, therefore, no part in the formation of this secretion, but passes the nodules unthickened and unaltered. Since, however, it is homogeneously stained with eosin, an appearance is presented as if the membrane of Bruch went past unchanged and without having any connection with the colloid mass (Plate XV, Fig. 4). Hence has arisen the view that these excrescences are in origin wholly independent of the membrane of Bruch. Staining with Weigert's elastic tissue stain, however, will be found to solve the problem, for the unaltered membrane will be found to be only the outer elastic layer of the membrane of Bruch, while the colloid body is a true bulging of the inner homogeneous portion, and like it does not stain specifically with Weigert.

The formation of colloid bodies, however, is not the only instance of a pathological process which affects the two layers in a different manner. In general the elastic layer is more resistant than the other to noxious influences, and in some cases of chorio-retinitis it will be found that in the situation of an inflammatory patch the homogeneous portion is eroded while the elastic layer still holds, or that when both have

"lamina *elastica*" for "membrane of Bruch." The point is merely one of nomenclature and not of great importance so long as the details of structure are kept clearly in view. Perhaps the most convenient way would be to follow Smirnow in calling the homogeneous portion the membrane of Bruch and the elastic portion the "supracapillary" layer of the choroid, reckoning it thus as the innermost stratum of the choroid, as no doubt it is developmentally.

ruptured the elastic layer can be traced for a considerably longer distance than the other. An excellent instance of the different reaction of the two layers to pathological influences will be found in a paper by Mr. Nettleship in the last volume of the Transactions of the Ophthalmological Society.* The case was one of sarcoma of the choroid, and on its summit, between it and the retina, there was a layer of "dense wavy fibrous tissue" passing peripherally into "a thin structureless membrane bearing the pigment epithelium on its inner (retinal) surface. This epithelium-bearing membrane seems at first sight to represent the elastic lamina of the choroid, but the latter structure is in reality separate from it, being traceable, with interruptions, from one side of the tumour to the other, as a very undulating, highly refracting line which lies for the most part in the substance of the sarcoma close to its inner surface; towards the margin of the tumour the elastic lamina and the membrane bearing the epithelium meet, coalesce, and pass on together to the choroid." A figure (Fig. 29) is given, showing very clearly the homogeneous or faintly laminated inner layer and the wavy strongly marked outer layer. Through the kindness of Mr. Nettleship I have had the opportunity of examining sections of these structures, and there can, I think, be no doubt that the "epithelium-bearing membrane" above described is nothing else than the homogeneous portion of the membrane of Bruch, indeed a large number of colloid bodies spring from it. The "very undulating highly refracting line," on the other hand is the outer elastic layer, and stains characteristically with Weigert's stain. The case, therefore, furnishes the strongest possible proof of the composite nature of the membrane of Bruch and of the origin of colloid excrescences from the inner layer of it.

The conclusion reached is therefore in favour of the deposition theory as opposed to the transformation. Both theories have, however, this in common, that they presuppose an abnormal metabolism in the pigment epithelium. What

* Trans. Ophth. Soc., 1904, vol. xxiv, p. 93; fig. on p. 100.

the stimulus or lack of stimulus may be, which results in this altered metabolism, one cannot presume to say. It is in part, no doubt, definitely pathological, since they occur very constantly in eyes, the subject of extensive destructive changes, but in part also it is to be regarded as almost a normal change, since they occur in a large proportion of senile eyes. Without wishing to draw any close analogy, a comparison may be instituted between these changes and the changes which occur in endarteritis. In the latter case also the lesion may be a definite response to a pathological stimulus (in the neighbourhood of gummata for instance), or may, on the other hand, almost be regarded as a normal senile change.

It may be of interest to append a short historical *résumé* of the growth of our knowledge of the minute anatomy of colloid bodies—touching only upon the chief works, for the literature of the subject is very great, and much of it does not require revival. The general conditions under which they occur need not be discussed, since this paper has not dealt with this aspect of the subject. They have been found in very numerous diseases of the eye, but probably stand in essential relation to none of them.

It is a curious fact that the much rarer outgrowths of the membrane of Descemet were described before those of the membrane of Bruch—by HASSALL, in 1849. Colloid excrescences were demonstrated in a single instance by WEDL, in 1854, but the first full description is by DONDERS, in 1855. Donders believed that it was the cell-nucleus which became the colloid body, and is the founder of the school which derives them by direct transformation from the pigment epithelium. In the same year HEINRICH MÜLLER had demonstrated them at a Würzburg medical society, and in the following year (1856) he published his views *in extenso* in a work full of careful observation and description, and still well worth a perusal. This was the foundation of the deposition theory, so that both schools were practically founded

in the same year. The intercalation of RUDNEW's work (1871) may be disregarded, but in 1874, Donders's original hypothesis was modified by DE VICENTIIS, who pointed out that the protoplasm was a more likely seat for the deposit of abnormal products than the nucleus, and this is the view with modifications of detail which has obtained among supporters of the transformation theory to the present time. The original form of the theory was speedily abandoned, and in 1876 DE WECKER states that the opinion "that these vitreous knobs arise by colloid degeneration of the nucleus of the epithelial cell seems to be entirely given up." Adhesion is given to this modified theory by DA GAMA PINTO (1882), DIMMER (1885), and DE BONO (1891). The best of these works is Dimmer's—the others need not be consulted.

Turning now to the development of Müller's theory, we find LEBER in several places steadily supporting it. MEYER also gives it his adhesion (1877). Ossification is first described by ALT in the same year, but the presence of connective tissue in the centre of the excrescence, a rare appearance, but one undoubtedly related to the occurrence of true ossification is only mentioned in 1895 by LEBER. Ossification is also shown in a plate in PAGENSTECHER and GENTH'S Atlas, but its exact position is doubtful.

In 1892 appeared an important work by KERSCHBAUMER, giving a description of the earliest appearance of the excrescences as homogeneous or finely granular thickenings of the membrane. It is here pointed out that there is no necessary correspondence in distribution between the colloid bodies and the changes in the pigment epithelium. The author, therefore, does not favour the transformation theory, and though it is not expressly so stated, may probably be reckoned an adherent of MÜLLER'S.

Coming now to more recent works, we find most of them supporting the transformation theory. In 1902 we have HOFMANN'S paper, with a new theory of origin as mentioned in the text. RUMSCHEWITSCH (1904) seems to believe that the excrescences commence as a deposit from the cells, but

that later the cell substance itself becomes transformed into colloid material. PES in the same year denies all connection with the membrane of Bruch, and gives their origin either as from transformation of epithelial cells, or from sclerosis of surface papillæ which he describes as the result of inflammation in the middle and outer layers of the choroid. Finally, SCHIECK (1904) is a supporter of the transformation theory.

Cases which have both been seen clinically and examined pathologically are rare in the literature. LIEBREICH described the first in 1858, and the only other which I have been able to find is one by NAGEL in 1875—the year in which HUTCHINSON and TAY described the condition since known in England as "Tay's choroiditis," which they correctly presumed to be due to these excrescences. I have in one case been able to observe them clinically in one eye, and to find them microscopically in the other eye of the same patient, and possibly this is not an uncommon experience.

It is impossible here to go fully into the literature of the normal structure of the membrane of Bruch, but the following papers may be merely mentioned. Most of the older accounts are founded on SATTLER'S (1876) description. Of recent investigations, especially with Weigert's stain, SMIRNOW'S (1899), should be consulted for the general structure. A very excellent description of its ending towards the ciliary body will be found in SALZMANN'S (1900) work on the zonula. Figures of its ending towards the papilla are given in a paper by SAGAGUCHI (1902), but his explanation differs from that given in the text. I omit all mention of the clinical aspect of the subject.

FIG. 1.

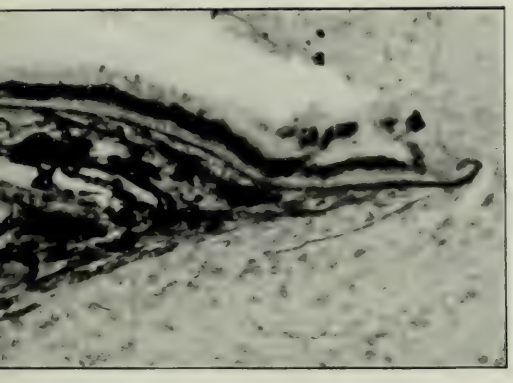

FIG. 2.

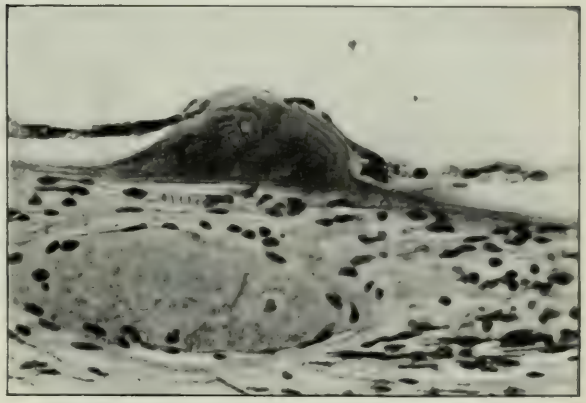

FIG. 3.

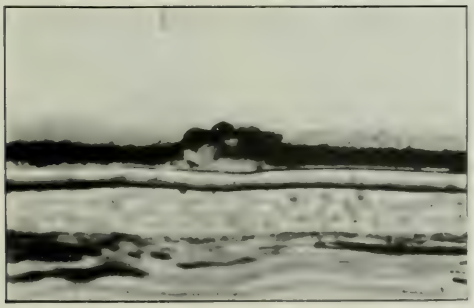

FIG. 4.

Bale, Sons and Danielsson, Ltd.

FIG. 1.

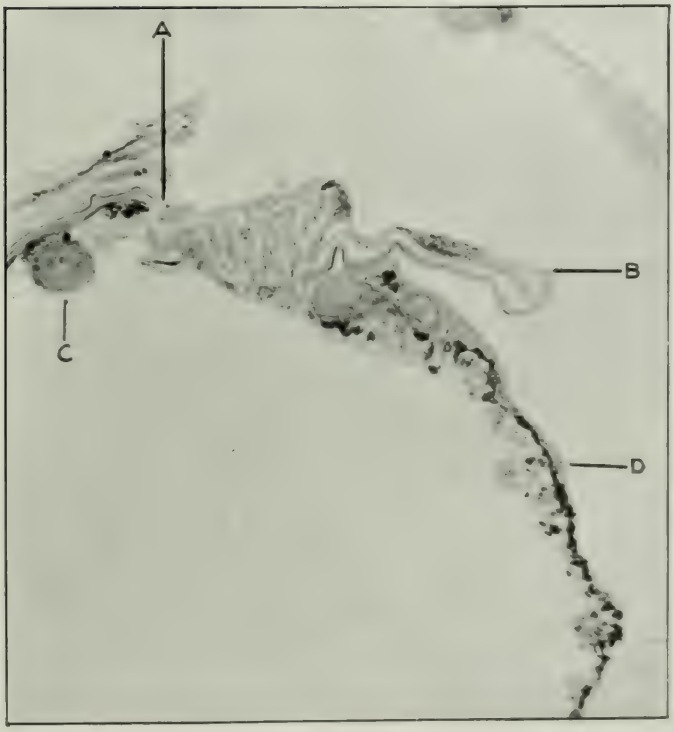

FIG. 2.

Bale, Sons and Danielsson, Ltd.

Description of Plates XV–XVI.

[I am indebted to Professor Wintersteiner, of Vienna, for permission to use the specimens from which Fig. 3, Pl. XV, and Fig. 1, Pl. XVI, were taken, and to Mr. Nettleship for the specimen photographed in Fig. 2, Pl. XVI.]

Plate XV, Fig. 1 (× 200).—Membrane of Bruch in the neighbourhood of the papilla stained with hæmatoxylin and eosin. It has a somewhat granular, but uniform appearance, and there is no division into layers.

Fig. 2 (× 200).—The membrane of Bruch at the papilla stained with Weigert's elastic tissue stain. It consists of an inner homogeneous or somewhat granular layer, and a thin deeply stained outer line. In the actual specimen this outer layer was coloured dark blue—the specific stain for elastic tissue. The two portions end differently, the inner at the same place as the pigment epithelium, while the outer projects for some distance into the substance of the papilla, and terminates in an upturned end.

Fig. 3 (× 200).—A colloid body stained with hæmatoxylin and eosin. It appears as a simple sessile bulging of the membrane of Bruch. It is covered by a single layer of flattened epithelium. In its centre there is a small clearer area, probably commencing degeneration (specimen by Professor Wintersteiner).

Fig. 4 (× 200).—A small colloid excrescence stained with Weigert's fluid. A strongly marked line runs past it, which is stained deep blue in the specimen and might be taken for the whole membrane of Bruch, of which however, it is only the outer part (*cf.* Fig. 2). The colloid body seems to have no connection with it.

Plate XVI, Fig. 1 (× 200).—Two large laminated colloid bodies stained with hæmatoxylin and eosin. Beneath them and apparently quite unconnected with them, there is a fine highly refracting zig-zag line. This is the outer elastic layer of the membrane of Bruch thrown into folds by the cicatricial shrinking which has taken place in the choroid (case of phthisis bulbi). Although the bodies are so large they are still covered by an unbroken but flattened and partially depigmented layer of epithelium (specimen by Professor Wintersteiner).

Fig. 2 (× 90).—(From a case of Mr. Nettleship's, reported in Trans. Ophth. Soc., vol. xxiv, p. 93.) To show the behaviour of the membrane of Bruch over a choroidal sarcoma. The two layers are well seen above, and from the inner homogeneous, a colloid body (C) springs. Their relations are here normal. At (A) the outer elastic layer breaks off suddenly. It reappears again as a zig-zag line ("very undulating, highly refracting line" of Mr. Nettleship's description), but ends finally at (B). The inner homogeneous layer (D), on the other hand, continues across the figure ("epithelium and 'colloid'-bearing layer"). Several colloid bodies are seen in it—the letter points to two small ones—and there were a number of others beyond the borders of this field and far away from the ending of the elastic layer.

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ON HEREDITY IN THE VARIOUS FORMS OF CATARACT.

By E. Nettleship.

The influence of heredity in causing cataract is mentioned by nearly all authors. Many single examples and small collections of cases have been published, more particularly in relation to the various congenital forms, as the list of references at the end of this paper will show. I do not know, however, that any considerable collection of material has been made by any one writer. Daust's Thesis (1899) [45] is one of the richest in cases that I have seen, and contains many references.

The following observations are based upon notes of my own cases, and of a certain number of published ones; but I have not attempted to exhaust the literature of the subject, and many other published records of familial or hereditary cataract might be found. I have purposely omitted reference to some of the very earliest published examples. In my own cases the informant has been, as a rule, a member of the youngest affected generation, and has been counted as having cataract for the purposes of this paper if striæ or vacuoles, however slight, were present in his or her lenses. My own material was obtained for the most part from educated patients, and their testimony on such a well-known condition as cataract may, I believe, nearly always be accepted.

It seems natural to begin by recognising two principal classes of cataract, (A) acquired or post-natal, and (B) congenital.*

The congenital class (B) is subdivided into lamellar, the much less common axial or spindle form, and complete cataract. Under the group of complete congenital cataract may fairly be included all cases of general opacity or opalescence of lens discovered within a few weeks, say two months, of birth, and also the cases in which a shrunken disc of opaque lens is discovered at the age of several months, or perhaps a year.

Class A of acquired—*i.e.*, post-natal—cataract contains, besides the ordinary senile forms, a præsenile or juvenile group in which the opacity comes on at various ages between childhood and about 40. This subdivision is, no doubt, arbitrary, and does not correspond with any differences in the cause or character of the cataract; but it has some practical conveniences.

The cases, often very distinctly marked, of disseminated cortical cataract, so common in young adults, characterised by dots and short blunt striæ, sometimes of blue colour, immediately beneath the capsule, and often least abundant at the anterior pole, are included for the present with the acquired cataracts, the cases being classified according to the patient's age. I do not know whether this form has been proved to be congenital, but all will agree that though the opacity often makes no visible progress for many years, it does occasionally increase to completeness. In certain examples there is great difficulty in distinguishing such cases from true lamellar cataract of slight degree (see Cases 76, No. 3, and 79).

If any important differences exist between the conditions governing inheritance or familial liability in one kind of cataract as compared with another, we may expect, I think,

* It must be admitted that cases are met with from time to time in which we cannot say whether the cataract was present at birth or came on during the years of early childhood.

that the division will correspond with the two main classes A and B.

Class A. ACQUIRED OR POST-NATAL CATARACT.

This consists of about 145 families, containing upwards of 500 affected persons. From 25 to 30 of the 145 pedigrees have been published, and several other very good ones have been given to me by Mr. Lawford, Mr. Fisher, and other friends; the remainder, upwards of 100, are from my own notes. The distribution of the cases was as follows:—

Senile Cataract.—Families, 122. Persons, 375; male, 145; female, 230.

These numbers show 38 per cent. male and 62 per cent. female, or at the rate of 1,536 females for every 1,000 males.

The 122 families are divisible as follows:—

Only one generation (siblings* only) known to have cataract—32 families containing 82 affected persons; 28 male, 54 female.

Two generations known to have cataract—63 families with 152 affected persons; 55 male, 97 female.

Three generations—26 families with 106 affected persons; 44 male, 62 female.

Four generations—4 families with 31 affected persons; 15 male, 16 female.

Five generations—1 family with 7 affected persons; all male.

Præsenile or Juvenile Cataract.—Families 25, persons 152; males 49, females 62; sex not stated, 41.

Only one generation known to have cataract (siblings only), 3 families containing 9 affected persons; 4 male, 5 female.

Two generations known to have cataract—13 families with 35 affected persons; 14 male, 21 female.

* Siblings, see footnote to p. 183.

Three generations—5 families with 38 affected persons; 11 male, 7 female, sex not stated 16.

Four generations—1 family with 12 affected persons; 5 male, 4 female, sex not stated 3.

Five generations—2 families with 40 affected persons; 15 male, 25 female.

Six generations—1 family, 18 cases, sexes given only in part.

The *total of both groups of Class A* gives 146 families with at least 545 persons; male 200, female 305, sex not stated 41.

One generation (siblings only)—35 families, 91 persons; male 32, female 59.

Two generations—76 families, 187 persons; male 69, female 118.

Three generations—31 families, 144 persons; male 55, female 69, sex unstated 16.

Four generations—5 families, 43 persons; male 20, female 20, sex unstated 3.

Five and six generations—4 families, 65 persons; male 22, female 25, sex unstated 18. (But in one of these genealogies (Case 18*a*) records have been kept of only the male members, the question having had reference to family property.)

The above data suggest certain questions from which the following conclusions may be drawn, although it is quite probable that some of them may be upset in future by a larger and more accurate series of records:—

1. When senile cararact occurs in more than one generation it is almost always continuous from one generation to the next (parent to child to grandchild, etc.) and appears very seldom to skip a generation. We must bear in mind, however, that continuous descent may not be so prevalent as it seems, for a cataractous grandchild (and it is from such that nearly all the pedigrees of three generations or more are obtained) would be less likely to hear of cataract in his grandparent if his own parent had been free than if that parent had also been affected. On the other hand, an

ancestor whose sight continued good in spite of some opacities of lens would be reputed by his family to have been free from cataract, and thus seem to break the chain of continuity which in reality he maintained by a feeble link. Collaterals,* uncles, aunts, cousins, are sometimes stated to be affected, and no doubt numerous collateral or indirect cases would be found if the histories were more complete.

In the much smaller group of præsenile and juvenile-acquired cataracts, of which I have found only 20 available pedigrees, yielding 49 childships,† the descent was also continuous in all except 3, in 2 of which the passage was from aunt to niece, whilst in the third (Maunoir's case of 4 generations) there was a break of *direct* descent in the second generation.

We may therefore say provisionally that when cataract, acquired at whatever age, occurs in more than one generation, it descends in the great majority of cases from parent to child, seldom skipping a generation; but that it is not uncommon for collaterals to be also affected.

2. A question allied to the last is whether in each childship the affected siblings occur in succession or are separated by unaffected children?

I have only about 9 *childships of senile cataract* complete enough to be of use in this connection. In 4 of these childships the cataractous children were born in succession, but 3 of these 4 occurred in one and the same pedigree (Heath, Case 19) of 4 generations; the fourth childship was in a pedigree of three generations in which the third generation inherited from both parents. (Case 1.)

* Some authors, *e.g.*, Bollinger, define *collaterals* as children of the same parents (Siblings), and use the terms *indirect* or *lateral* for inheritance from grandparents, uncles, and aunts, *direct* inheritance being from parent to children.

† "Childship;" Dr. E. Stainer's term to express all the children of one parentage. The word Siblings is used in the same sense by Karl Pearson, and though to my ear less euphonious, is sometimes more convenient. I propose to use these terms indifferently.

KEY TO THE SIGNS USED IN THE FOLLOWING PEDIGREES.

♂, *Male unaffected.* ♂, *Male with cataract.*

♀, *Female unaffected.* ♀, *Female with cataract.*

○, *Sex not stated unaffected.* ●, *Sex not stated with cataract.*

◯, *Several Children free from cataract.* When all are of the same sex the sex-sign is added to the circle; numbers, Roman or Arabic, within the circle indicate the number of such children.

Parents joined by a bracket, above or below, are cousins; thus ♂ ♀ or ⌒

Brothers or sisters joined by a horizontal line are twins: thus ♀—♀.

Siblings (Professor Karl Pearson), *Childship* (Dr. E. Stainer).—Synonymous terms indicating the entire offspring of one parentage, used instead of "brothers and sisters;" miscarriages and still-births are included when known.

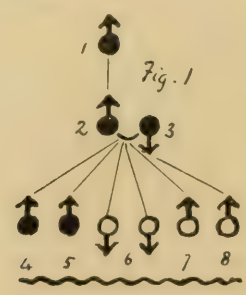
Siblings when not underlined are in their true order of birth, the first-born being at the left-hand end of the line.

A wavy line (~~~) *beneath a childship* means that the order in which the members were born is not known.

Successive generations are indicated by Roman numerals (I, II, III, etc.), or occasionally by letters (A, B, C, etc.), placed at the side of the diagram.

N.B.—In such of the published cases as contain the facts in "tree" form, I have copied the authors' pedigrees, but, for the sake of uniformity, have substituted the signs in the above key. But when, as in the great majority of published cases, no diagrams are given, I have constructed the figures from the authors' statements.

CASE 1 (Fig. 1) (51,171).—Showing continuity and double inheritance of senile cataract.



1. Grandfather had cataract. 2. Son of 1. 3. Wife of 2; both these had cataract; they were not cousins.

4 to 8. Children of 2 and 3, in order of birth.

4. Mr. B., 51,171, cataract diagnosed, æt. 57; when 59, R. was complete, L. incomplete (1899). 5. Operated for cataract with success; still living in 1899. 6. Two sisters; good eyes. 7. Son, died of heart disease. 8. Son, drowned.

Of *childships of Præmature and Juvenile Cataract*, I have found 11 that bear on the point; in at least 7 of them the cataractous children were born in succession. Berry comments on this point in his own case (Case 27, below), and observes that the tendency of the cases of cataract to appear in successive siblings is apparently caused by a greater tendency to transmission by the mother at some particular period of her child-bearing life than at others.* He further noticed that in his case the eldest girl of an affected childship never escaped.

If any conclusion were permissible from such small numbers it would be that when several siblings in succession suffer from acquired cataract, the liability to cataract will be found to have run through several generations, or to have been intensified by inheritance from both parents.

3. Does hereditary acquired cataract descend more frequently through the father or the mother?

In the group of senile cataract I have about 112 instances of transmission from parent to child, using each 2 generations (1st to 2nd, and 2nd to 3rd) separately.

In 67 of these instances the tendency was transmitted through the mother, in 45 through the father, *i.e.*, it descended more often through the mother than through the father in the proportion of about 1,466 mothers to every 1,000 fathers.

I do not attach quantitative value to these figures. In

* Sir William Adams (2*b*) observed as long ago as 1817 that in his experience when *congenital* cataract affected more than one member of a childship, the affected children were always in succession, and he gives two illustrative cases, one of them of three generations (Cases 84 and 91 below).

the first place, the numbers are very small; secondly, we must allow for the greater difficulty experienced, from sundry causes, in obtaining family histories from men and concerning men, than from and concerning women; lastly, a decided preponderance would be expected in women owing to the woman's greater expectancy of life.

Whether these various sources of error do or do not explain the whole of the above stated excessive frequency of hereditary senile cataract in women as compared with men cannot at present be determined; either thesis might be defended.

In this connection we need to compare (1) the sex frequency in hereditary cataract with (2) the sex frequency in similar cataract with no history of heredity; and (3) with the sex frequency at the corresponding ages (say 45 to 85) in the population from which the patients with cataract are drawn. No fair comparison can be made at the present time between any two of the above three terms; the collection of material for deciding No. 1 is only in its infancy; no attempt to decide No. 2 is possible until family histories have been taken by routine in a large series of cases; and as to No. 3, some idea of its complexity may be gathered by an inspection of the Report of the Census of England and Wales for 1901. From this Blue Book we learn that (*a*) the proportion of females to males has gradually increased from 1,036 females to every 1,000 males *of all ages* in 1821, to 1,068 females in 1901; (*b*) that the sex frequency varies widely in different districts of the country, and even in different parts of London, the excess of females being much above the average in some of the southern counties and in London as a whole; (*c*) that between the *ages of* 45 *and* 85 the sex frequency shows similar variations both as to dates and localities; and that in the counties most likely to send their cataract cases to London, and in London itself, the proportional number for women within those ages in 1901 varied between 1,164 and 1,209, say about 1,175.

Even the incidence of senile cataract as a whole in the

two sexes cannot be determined so easily as one would suppose, and no doubt such disturbing factors as those just alluded to will explain many of the widely different statements on this subject that are to be found in literature. In regard to London experience, the following figures may serve as a starting point. I have ascertained the sex in 4,283 persons operated upon for senile cataract during a series of years at Moorfields, St. Thomas's, and St. Bartholomew's Hospitals, and from my own private practice, and find that 2,370 (56 per cent.) were women, and 1,913 (44 per cent.) men, or 1,240 women to 1,000 men. Though a large number of these patients were, of course, from London or the "Home" Counties, a considerable sprinkling came from many different and more distant parts, and as the corresponding proportional numbers for all England and Wales (1,142) and even for the "Home" and London district (say 1,175) are notably less than 1,240, it seems fair to conclude that in our country women are probably somewhat more liable to senile cataract than men, and that this greater liability, together with the woman's greater expectancy of life, may explain the relative frequency of descent of familial cataract through the mother that has been referred to on p. 185.

But if, departing from mere numbers, we examine only the longer pedigrees of senile cataract—of three generations and more—in their entirety, *i.e.*, without taking successive pairs of generations separately (1st to 2nd, 2nd to 3rd, etc.), the relative frequency of descent through the female is very striking. I have 26 available pedigrees of 3 generations or more. In 8 of these the descent was invariably from female to female to female, and in 5 others a female transmitted in nearly every case. In only 4 families did descent occur from male to male to male.

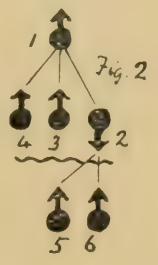
Then I have one case (Case 29) of 2 generations in which the mother, marrying twice, had a cataractous daughter by each husband.

In the præsenile group a similar preponderance of descent

through the mother appears, though the numbers available are small; in 46 instances of transmission, descent was through the mother in 27, through the father in 19.

At this point attention may be drawn to the interesting fact that in certain stocks of senile and præsenile cataract the disease has a special tendency to select one sex to the exclusion of the other: in one stock all, or a marked majority of, the affected persons being males, as in the examples on the following pages; in another stock all or the great majority being females. It seems doubtful whether either sex has a marked preponderance to this tendency, for whilst in 9 such pedigrees all the cases, and in 4 others a majority, occurred in males; in 7 pedigrees all the cases, and in 10 others a majority, were in females. This special liability of one sex or the other to suffer exclusively in certain families is also well illustrated in some of the congenital cases:—thus in Galezowski's "Incomplete lamellar" family (Case 66) 3 generations gave 7 patients all females; whilst in Dyer's case (Case 81) of unknown kind, but not improbably lamellar, cataract occurred only in the males (about 10 cases); Müller's Case (Case 78), and Appenzeller's Case 6 (Case 85 below) both congenital forms, also show this feature. Arago [23] makes the same point when he suggests as a working hypothesis in discussing his own præsenile case (Case 39) that "hereditary cataracts are transmitted by preference to individuals of the same sex as the one first affected;" this is true in some cases, but exceptions are common.

In the following cases nearly all the sufferers were males:—



CASE 2 (Fig. 2) (J., 36,179).—Cataract in 6 members of 3 generations, all the cases except 1 being in males.

1. Had cataract.

2. A daughter, born 1818, and operated for cataract when 63 years old. Had 2 sons with cataract (below).

3 and 4. Two brothers of No. 2 who had cataract.

5 and 6. Sons of 2.

5. Mr. J. J. Cataract diagnosed at age of 46.

6. Mr. R. D. J., born 6 years after No. 5. Cataract diagnosed at age of 47; rapidly matured, and was extracted at age of 49, with good result.

CASE 3 (Fig. 3).—Galezowski [21]. Cataract in 4 generations, the first patient being a woman, but all the subsequent ones men.

In Ziem's case (Case 47) of juvenile familial cataract the males suffered in 4 successive generations, but apparently no females were attacked. But in one of Sichel's cases (Case 40 below) in 3 generations females suffered exclusively.

4. Another question—Is hereditary acquired cataract usually transmitted to the same sex or the opposite?

Examination of the senile and præsenile groups together shows that according to my figures the sex of the cataractous subjects remains the same in each succeeding generation in somewhat more than half the cases and changes in rather less than half.

The conclusion from what has been said as to sex in relation to descent in acquired cataract is that after making a large allowance for survival, for imperfection in note-taking and for other sources of error, females are probably somewhat

more liable to familial acquired cataract than males, and that the disease is derived more often from the mother than the father; but that it is transmitted by the predisposed or affected mother to her sons nearly, perhaps quite, as frequently as to her daughters.

5. Another question is whether hereditary senile and præsenile cataract shows a tendency to appear earlier, or at least to mature earlier, or later, or at about the same age, in each succeeding generation? The data for answering this question numerically for the senile group do not exist, but a number of instances illustrating one or another of the above occurrences can be quoted.

The following cases appear to show earlier incidence or "anticipation"* in the younger generation:—Case 2 (p. 189) is a good instance. The following are further examples:—

CASE 4 (44,218).—Father, operated for cataract when past 60.

Son, symptoms recognised æt. about 47; complete in one eye æt. 48, when it was operated with good result.

CASE 5 (49,101).—Father operated for cataract, æt. 68. Had 8 children.

No. 1, son, both eyes operated for cataract, æt. 49; good result; living, æt. 51.

No. 8, son, cataract began æt. 35; æt. 36 seen with extensive posterior cortical opacities.

Nos. 3 and 6, both sons, died of renal and vascular disease respectively, one being very alcoholic.

CASE 6 (39,221).—Father operated for cataract, æt. 50.

Cataract began in son, æt. 35, and nearly complete in one eye at 40.

CASE 7 (T. I. P., 1885, 150).—Father, cataract in old age.

One son and two daughters all operated for cataract at or before 50, and all did well.

* "Anticipate;" the term used in describing cases of ague in which the attack begins at an earlier hour in the day than did the attack that immediately preceded it. (Bristowe, Theory and Practice of Medicine, 7th edit., p. 288.) The term may be used in the present connection by substituting years for hours and, for successive attacks, persons of successive generations.

Case 8.—For this example I have to thank Mr. Lawford :— Thomas R., sight began to fail æt. about 46. When 48 (1903), R. cataract complete, and extracted with good result; L. incomplete. His father had cataracts removed when æt. 70.

Case 9 (55, 22).—Mother, preliminary iridectomy 1896, when she cannot have been much less than 60, for her daughter was then æt. 40. This daughter also had preliminary iridectomy in 1898, when she was 42.

Case 10 (50, 123, and 124).—Father, cataract diagnosed in L., æt. 55 : seen, æt. 57, with nuclear haze in L. R. lens clear (June, 1899).

Daughter, æt. 21 at above date, had fine marginal opacities and scattered vacuoles in both lenses.

Case 11 (45, 111, and 112).—Mother, æt. 53, abundant fine vacuoles and striæ in lower part of each lens, not interfering. V. 6/5.

Daughter, æt. 27, fine dots on back of R. lens, and a single one on back of L. Slight interference with V. for a number of years.

Case 12 (43, 70, and 46,141).—Mother, cataract diagnosed about 65 ; still very incomplete but increasing æt. 72.

Daughter, striæ and vacuoles, æt. 28.

Case 13 (14, 33).—Mother's cataract diagnosed when she was æt. between 30 and 40 : progress very slow and not complete 30 years later, when cataract was diagnosed in her son, æt. 39. In this son it became complete in one eye, and advanced in other when he was 42.

Case 14 (21, 117, and 14,124).—Mother said to have had cataract when quite old, and was blind (of it) for 3 years before she died, æt. 90.

Two daughters, cataract began about 60, and operated by me, æt. 64 and 68.

One daughter, operated long ago for cataract, which came when a girl.

One brother had cataract, æt. about 30 ; was operated, and saw well ; now dead.

One brother, now (1887) æt. 60, blind of cataract for many years and insane.

CASE 15.—Louis Stricker [81] saw double cataract develop in a woman at the age of 57, in her daughter at 48, and in this daughter's daughter at 26.

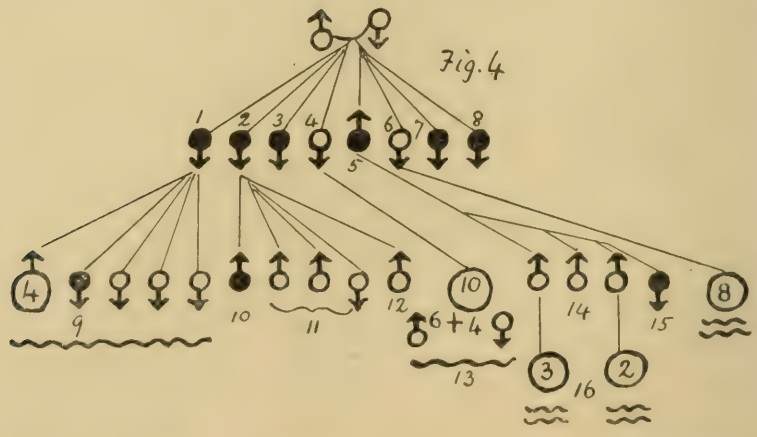
CASE 16.—Appenzeller [24] mentions (as his Case 8) that cataract formed in a woman at the age of 54, her son became blind of cataract at 35, and in a daughter younger than the affected son cataract began at 24, and became complete in about a year.

In Case 29, early posterior-cortical cataract found in father, æt. 31; in son, æt. 24.

In Case 30, posterior-cortical cataract diagnosed in aunt, æt. 36, but probably then of several years' standing. Similar cataract began in two of her nieces (themselves sisters) at about æt. 8, and became complete soon afterwards.

In Case 31, dotted cortical cataract was diagnosed in the mother, æt. 32, and 9 years later in her daughter, æt. 14; but it was probably present in the daughter at least 5 years before, if not at birth.

Sichel's (fils) [16] cases (Cases 40 and 41) and Froebelius's [8] (Case 90) appear to illustrate the same point.



CASE 17 (Fig. 4).—Nine cases of senile cataract in 2 generations. Incidence earlier in second generation (P. and T., 22,231).

Generation I—

1, 2, 3, 5, 7. Cataract began in these at about æt. 65; four

of them died at ages from 69 to 81, only one (No. 7) still living, æt. 82 (1902). Cataract very slow in all, and none were operated. (No. 3 = P. 7,151.)

8. Cataract began about 60; operated with success, æt. 63; died, æt. 67, many years ago.

Generation II—

9. The eldest of the 4 daughters of No. 1; cataract began æt. 50 to 60; still living, æt. 70, in 1902, and cataract still not mature.

10. First-born of No. 2; cataract began æt. 45; both operated, æt. 51 and 54, successful; æt. 56 in 1902. (22,231.)

11. All living, æt. 54 to 49, in 1902, and no cataract.

12. Ob., æt. 26, accident.

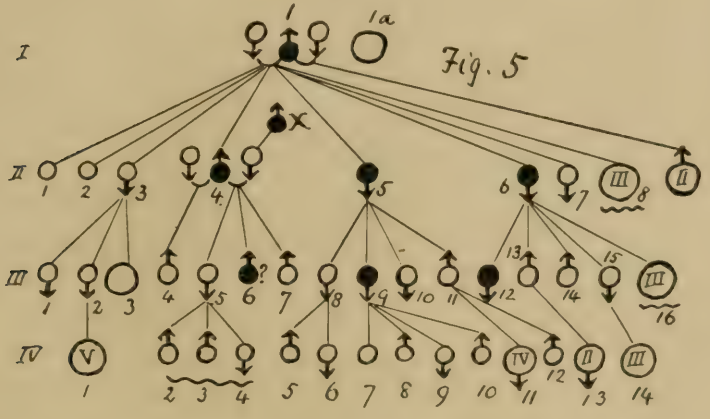
13. Ten children of No. 4, 6 male, 4 female, none cataract.

14. Unmarried. No cataract.

15. Unmarried. Slight changes in lens, æt. 39, in 1898. In 1904 = æt. 45, opacity not increased. (45,168.)

16. These are still children (1902).

I have seen Nos. 3, 10, 14, and 15.



Case 18 (Fig. 5).—The Vesey family. Six (probably 7) cases of early senile cataract in 3 generations. (T.I.P. 1885 and 1897 also notes from Mr. Jessop.)

Generation I—

1. A working jeweller had to give up work about æt. 50, or earlier, from failure of sight, which was always spoken of by his children as cataract. Was not operated. Died between 50 and

60 years of age. He was one of several siblings (1*a*), but nothing is known of the others. He married twice; his wives not cousins either to him or to each other. By 1st wife, 10 children, of whom Nos. 4, 5, and 6 had cataract. By 2nd wife, 2 sons; both died young.

Generation II (by 1st wife)—

1 and 2. Died in infancy.

3. Daughter. Good eyes.

4. Fourth born (son). Both eyes operated for cataract, æt. about 45, and did well. Died æt. about 55. Married twice; the wives not cousins to him or each other. By 1st wife 1 son (III, 4). By 2nd wife 1 daughter, then 2 sons (III, 5, 6, 7); one of the four probably has cataract. The first-born by second wife (III, 5) had 3 children (IV, 2, 3, 4) who see well hitherto. The 2nd born (son, III, 6), now (1905) middle aged, has progressively failing sight, which his cataractous relations (II, 5, and III, 9) tell me they have no doubt is due to cataract; he refuses to be examined. X., the father of the 2nd wife of II, No. 4, is known to have had cataract, and died an old man without operation; therefore III, No. 6, inherits from both sides.

5. Mrs. Vesey (5th born). R. operated for cataract by myself, æt. 50 (1885); symptoms began about æt. 45. L. operated, æt. 57. Both did well. Now æt. 70 and sees well (1905). Has 4 children, of whom the 2nd has cataract (III, 9, below).

6. Emily (6th born). Both eyes operated for cataract, æt. about 40; cataract began about æt. 38. Has 7 children, of whom first-born (daughter) has cataract (= III, 12).

Generation III—

6. Probably has cataract (see above).

9. Mrs. Carter. Second born and 2nd daughter of II, 5. V. failed about æt. 38, 15 years after marriage, and 7 years after birth of youngest (4th) child. R. operated for cataract (Mr. Lawford), æt. 41 (1904), did well. L. incomplete cataract.

12. Mrs. Airs. First-born of II, 6 (Mr. Jessop's patient). R. began to fail, æt. 32, and Mr. Jessop extracted cataract, æt. 33 (1894). L. followed, beginning chiefly at posterior

cortex, and was extracted by Mr. Jessop, æt. 36 (1897). Both did well. Married 20 years, no children. Now æt. 43 (1905).

None of Generation IV, who are still all children, have as yet shown signs of cataract.

Case 20.—Mr. Lawford and Mr. Fisher have given me the following case of 4 generations :—(T.I.P. 1894. No. 42.)

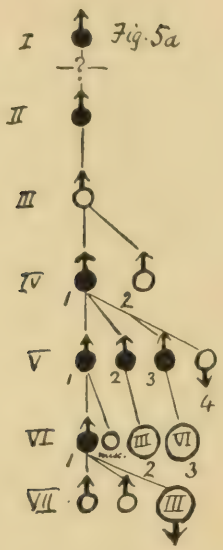
Annie S., first-born of 9. Sight began to fail, æt. 23. L. cataract removed, æt. 26 ; R. cataract removed (by Mr. Lawford), æt. 30 (1894).

Her mother, mother's mother, and mother's mother's mother all suffered from cataract comparatively early, and each was, like the patient, the eldest *daughter* of the respective childship. "In each generation the cataract appeared at an earlier age than in the one preceding it," but no particulars of the ages are given except for the patient (= 4th case).

It is, however, not uncommon to find that the cataract has come on at about the same age in all the affected members of a family. Bowman observed this, and it has been mentioned by others. In many such instances another feature, alluded to by Fuchs and others, has been the comparatively early age at which the malady has appeared in all the sufferers. Such a frequency of præsenile cases in family cataract does not, however, of itself prove that the hereditary tendency is more liable to manifest itself at an early age than in advanced life, for the greater the longevity of each generation the greater is the difficulty, other things being equal, of obtaining records of past generations.

The following cases illustrate the above points :—

Case 18*a*.—Mr. ——— (Fig. 5*a*, VI, No. 1), æt. 55, Mr. Lawford's patient at St. Thomas's Hospital ; cataract coming about a year and a-half ; extraction of R. with good result, April, 1905. Five children (2 sons and then 3 daughters) ; none have shown signs of cataract. He knows about his direct male ancestry for 5 generations back, but not the female and collateral members ; the pedigree is as follows :—



I. Male, had some disease of eyes called cataract about the year 1730.

My informant was not quite certain whether the next generation was son or grandson of I; if there was an intermediate there is no history of his having had cataract.

II. Colonel —— fought at the Battle of Culloden in 1745, and having afterwards to leave the country, lived for the rest of his life in France, where he worked as a bricklayer near Paris. He became blind from cataract, and was operated upon in Paris, probably about 1780, when aged 60 to 65. His eldest son (III) is not known to have had cataract, but his history is really lost. III had two sons :—

IV. 1. Eldest son of III. Cataract. Was a florist near London. Was operated on with good result when about 60, and lived to be 93.

2. George, believed not to have had cataract.

V. Children of IV, 1—

1. Eldest son, George, operated for cataract at Moorfields by Mr. Tweedy at the age of about 53 and lived to be 84.

2. John, also operated by Mr. Tweedy at about the same age and lived to be 76, dying in January, 1905.

3. Alec, 3rd brother, operated by Mr. Tweedy when rather more than 50, and died æt. 70 in 1904.

All the above did well after the extraction.

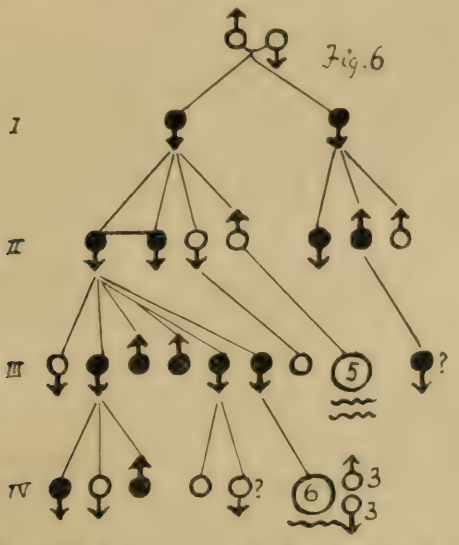
4. Daughter, emigrated when young and not heard of since.

VI. 1. The patient, only living child of V, 1; there was 1 miscarriage.

2. Three children (2 male, 1 female) of V, 2; none have cataract.

3. Six or 7 children of V, 3; all believed to have good eyes.

VII. Five children of VI, 1 (see above).



CASE 19 (Fig. 6) (14, 54 and T. I. P., 1888, Heath).—Mixed senile and præsenile cataract in 4 generations. No clear evidence of earlier incidence in the younger generations.

The ages of the two cataractous persons of generation I are not known.

The ages of 3 out of the 4 cataractous persons of generation II were "old age," "about 80" and 50 respectively; age of the 4th not known. Note that both the twins were affected.

The ages of the 5 cataractous ones of generation III were—

about 50	when	operated on in	2
30	,,	,,	1
65	,,	,,	1
50	when	diagnosed ...	1
			5

In generation IV there were 2 cases—

Cataract beginning at 40 in		1
„ operated	„ 33 „	1
		2

There were 13, perhaps 14, cases in all, and of these 7 are known to have been operated. No fresh cases have occurred in Generation IV since 1888.

No consanguinity known; but all the patients lived within 10 miles of each other in an agricultural county (Lincolnshire), where the family had been settled for a long time.

Case 21 (51,166).—Cataract began in mother at about 35 to 40, and in daughter, æt. 30 to 35. In mother V. was still pretty good, æt. about 50. The daughter's was the cortical dotted form with some blue opacities; of the mother's, no particulars are given.

Case 22 (35, 26).—Mother operated for cataract, æt. 89.
Son, early changes, æt. 70.

Case 23 (29,132).—Cataract very slow in mother, now æt. 92, and son, now æt. 70.

Began at about 60 in son, and may have done so in mother.

Case 24 (17,147).—Mother and daughter; cataract very slow in both.

Daughter not much worse æt. 72 than 50.

In Hirschberg's[11] case (Case 34) of 3 generations the cataract was observed at about 28 in all but one of the subjects, and operated at 30 to 35.

In Klamroth's[12] (Case 35) it came between 21 and 23 in father and his twin sons, and was operated at 29.

Other cases, illustrating onset at about the same age in each generation and described further on, are those published by Schanz (Case 26), Streatfeild (Case 28), Tatham Thompson (Case 36), Appenzeller (Case 38), Arago (Case 39), and my own Cases 32 and 33.

There appear to be but few cases in which cataract

comes on at a later age in the succeeding generations. The following is one:—

CASE 25 (47, 89).—Mother operated for cataract, æt. 50.
Son, cortical opacities, æt. 54.

It seems from the foregoing facts that *there is some tendency for hereditary cataract, both senile and præsenile, to appear earlier, or, at any rate, to ripen earlier, in the younger generations.* But evidently great differences in this respect occur between different families,* and even between different members of the same childship, and the point is one upon which fuller and more accurate information is much to be desired. Certain cases (*e.g.*, Case 34) raise the question whether "Anticipation" if carried far enough may not reach the child *in utero,* and thus lead to some form of congenital cataract.

6. When *senile cataract* affects several siblings, does it come on at or about the same age in all?

In Case 19 (Heath family) the cataract is said to have come at about 50 in 4 of those affected in the 3rd generation and at 30 in 1, that one being the 5th born of 6 and dying of phthisis at 38.

In Case 17 (P. T. family) no marked difference of age at onset was known: the cataract came on at about 65 in the 5 elder of the 6 cases in Generation I, but began decidedly earlier, or ripened decidedly earlier, in the 6th patient, who was the 8th born of 8 (began 60, operated 63).

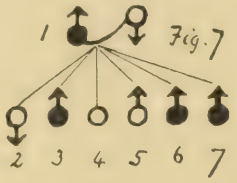
Cases of Præsenile and Juvenile Acquired Familial Cataract illustrating some of the preceding Questions.

Cases 19 and 20, already given, belong to this group.

CASE 26 (Fig. 7).—Schanz [20] published the following case of cataract coming on in the twenties in 3 brothers, whose father

* Galezowski (21) has a very similar remark on this subject in Rec. d'Ophthalmologie, 1882, p. 719, etc.

probably had cataract developing when he died, æt. 40. It is just possible that in the youngest subject (No. 7) the cataracts were self-made, in order to escape military service, but this does not apply to No. 3.



1. Father, died at 40 of lung disease. Sight defective during the last years of life, and was told an operation would be needed later. Could see to work till the last.

2. Girl (1st born), died æt. 7, in consequence of a fall.

3. (2nd born) Julius P. Passed army tests; afterwards sight became dim, æt. 26, in R., and then L. Both matured rather quickly. Operated before æt. 30. No fits.

4. (3rd born), died, æt. 2; said to have had disease in neck, and swellings on arms. Sex not given.

5. Son (4th born), died, æt. 13; cause not stated.

6. Josef (5th born). History of corneal ulcers and scrofulous glands. Sight pretty good till æt. 18, when he rapidly became blind. Not seen by author, but cataract inferred (æt. 26 in 1897).

7. Son (6th born), æt. 23 (1897), a tailor. Sight quite good till about æt. 22. Then rapidly forming cataract in R.; becoming complete in *two months*. L. rapid also, and operated within a few weeks of operation on R. Note that this man had been put back from beginning his military service for a year for general debility and that the cataracts formed rapidly (2 months) during that year.

No sugar or albumen in any of the patients.

Case 27 (Fig. 8).—Berry [25] published in 1888 what is probably the most remarkable example of hereditary cataract hitherto recorded, 55 individuals, spread over 5 generations, furnishing no less than 20 cases. In all the cases the cataract developed in early life, usually in childhood (æt. 7 and 9 in 2 cases), occasionally in adolescence (æt. 18 in 1 case). It became complete. The pedigree (Fig. 8), is from Berry's paper, but my own signs

have been used. In no case did the eldest girl in an affected childship escape.

CASE 28 (Fig. 9).—In 1858, Streatfeild[7] published the following case:—

1. Mother. Cataract discovered, æt. 1½. Operated incompletely. Was æt. 33 when seen.

2. Cataract came on, æt. 6. Operated; æt. 16 when seen.

3. Died, æt. 5; no known defect of sight.

4. Cataract operated; æt. 11 when seen.

5. Cataract not operated; æt. 9 when seen; grey opalescent cataracts.

7. Cataract not operated; æt. 5 when seen; diffuse cataract not so advanced as No. 5.

8. Cataract began, æt. 1½; not operated; æt. 3 when seen; opacity chiefly at lower part of lens.

9. No cataract; examined when æt. 8 months.

The cataract in all cases said to have come on so rapidly as to cause practical blindness in 4 to 6 weeks, sight having been previously good. In the eldest (No. 2) sight was good till æt. 6; in No. 8 only till æt. 1½. Mother and all affected children grey irides and very light hair, almost colourless in the younger ones. Colour of eyes and hair probably same in the unaffected children as in those with cataract. Mother, eldest of four, has two sisters and a brother with brown eyes and good sight. No nystagmus in any. All good health, and well nourished.

CASE 29 (Fig. 10).—Palmer (15,147 and M., I.P. 1889) :—

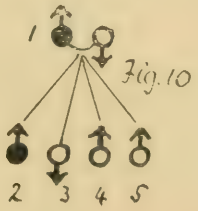


Fig. 10

1. Father. Posterior cortical cataracts diagnosed, æt. 31 (1887). Both complete, æt. 33, and operated with success (1889). 1904, æt. 38, V. keeps good.

2. First-born of No. 1. Sight began to fail at æt. 24 (1904), when Mr. Fisher found posterior cortical cataract.

3. Æt. 18 (1904).

4. Æt. 15 (1904).

5. Æt. 13 (1904). Wears weak + glasses for hypermetropia.

CASE 30 (Fig. 11).—Culverwell (T.I.P., 1885, and O.P. letter) :—

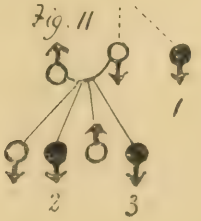


Fig. 11

1. Aunt (? maternal or paternal). Posterior cortical cataract, both, æt. 36, with R. 6/18 not improved, some old choroiditis;

L. – 3 D., 6/9, some old choroiditis, and less opacity of lens than R. R. failing since, æt. 20.

2. Grace Culverwell. V. thought to have always been bad. Æt. about 9 (1885), posterior cortical cataracts. L. needled, curetted, and suppurated. 12 months later (1886) R. preliminary iridectomy followed by extraction in two months; purulent iritis and shrinking of globe. No fits. Teeth normal. A long illness with vomiting whilst teething. Measles and whooping cough, æt. 2 years.

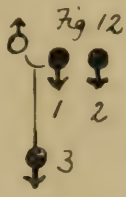
Mother pulled down by nursing husband with bad typhoid towards end of pregnancy.

3. Ellen. Cataracts chiefly posterior cortical, found æt. 8 (1888), getting worse; had seen quite well, æt. 4. No operation.

4. Æt. 11 in 1885; good sight.

5. „ 7 „ „

Case 31 (Fig. 12).—Bt. (36,178):—



1. Mrs. Bt. Dotted peri-nuclear and cortical cataract diagnosed, æt. 32. No definite history, but always slightly myopic. Only seen once (1889).

2. Sister of Mrs. Bt. (= Mrs. Bl.). Peripheral striæ, chiefly below, æt. 30 (1895). Only seen once.

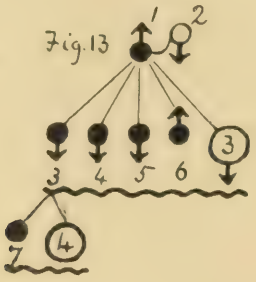
3. Daughter of No. 1. Similar dotted cataract diagnosed, æt. 14 (1898).

Case 32 (M., 53,100).—1. Grandfather; cataract in both, æt. 36, operated several times with poor result. Lived to be 84.

2. Mother; free.

3. Daughter (Mrs. M.); cataract diagnosed in R., æt. about 35. When seen, æt. 38 (1900), half complete. L. had marginal opacities æt. 38. No cyclitic signs in either eye.

CASE 33 (Wood, T.I.P., 1881, No. 79) :—



1. Operated for cataract when a young man, and wore glasses after. Died, "brain-fever," æt. 43.

2. Wife of No. 1 ; good sight. Died, bronchitis, æt. 79.

3. Lydia Wood.—L. cataract began about æt. 33 ; operated in the country æt. 35 ; did badly and went into secondary glaucoma. R. began about æt. 35 ; extraction of softish but much shrunken lens (St. Thomas's Hospital) æt. 40 ; scoop extraction and loss of rather thin vitreous ; 5 weeks after operation V. 6/12. Health and previous history good.

4 and 5. Two sisters died in early childhood ; both said to have cataract.

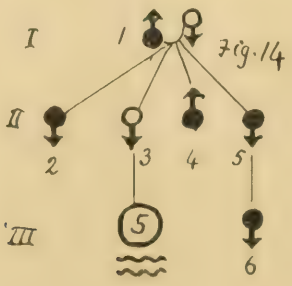
6. Brother now (1881) nearly blind from cataract ; age not stated.

Then came 3 sisters, of whom 2 living (1881), near-sighted but see small things well ; the 3rd died, æt. 37, after a long illness.

7. Child (? sex) of No. 3. Blind in one eye ; no history of inflammation or ophthalmia ; doctor said "cataract." Died æt. 18 months of whooping cough.

Then 4 other children of No. 3, healthy and see well.

CASE 34 (Fig. 14) (from Hirschberg [11]) is as follows :—



The parents of Generation I had good sight.

1. Samuel E. was operated for complete cataract with success when æt. 30.

2. Had one eye operated for cataract by v. Graefe æt. 28. Seen by Hirschberg æt. 41 (1874); operated eye good, other complete cataract.

3. Good eyes æt. 38 (1874). Has 5 children, all free from cataract.

4. Sight began to fail æt. 28; had previously seen well enough to go through his military service. Now (1874) æt. 36 double cataract ready for operation.

5. Cataract formed at about æt. 28. Seen æt. 29 (1874) with cataract complete in L., and nearly so in R. L. extracted with perfect result.

6. Daughter of 5, æt. 12 months (1874); double "congenital lamellar" cataract, for which iridectomy performed. A fine healthy child.

The history of this family was that sight was quite good in Generations I and II till about the age of 28. No sugar in urine. The men were all big and strong.

CASE 35 (Fig. 15).—In the same year Klamroth [12] published the following example:—

1. Father, cataract came on at about the same age as in his 2 sons.

2 and 3. Twin sons of 1.

In No. 2, a labourer, cataract began at about æt. 21 and got gradually worse. At 29 (1874) L. operated with good result.

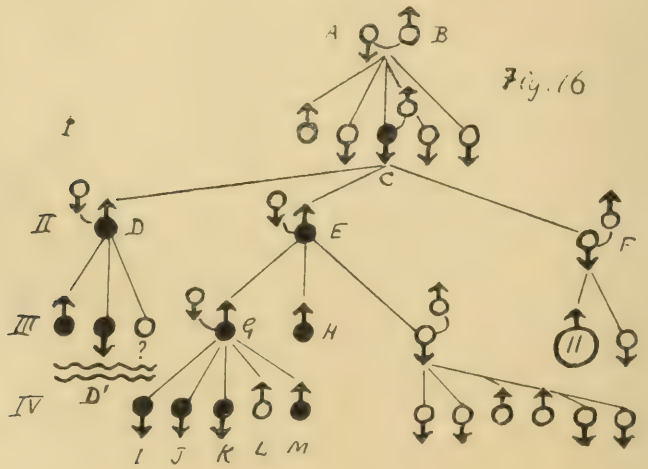
In No. 3 the cataract began at about æt. 23 and at 29 was complete in L. and incomplete in R. Operation with good result.

The twins attributed their own disease to the heat from brick-

kiln at which they worked; but author thinks the brick fire was not enough to cause it. No mention of father's occupation.

CASE 36 (Fig. 16).—The following example of cataract coming on in childhood in 4 generations was published by Tatham Thompson[37] in 1890. The opaque lens in some of these cases was remarkably hard, in fact, allied in texture to cataract of older people.

The pedigree is copied, with slight modifications, to suit my own "key," from Thompson's paper :—



A and B. Had no cataract.

C. Cataract came in childhood; operated, æt. 12.

D. Became blind with cataract, æt. 5, and was operated.

E. Became blind of cataract and operated, æt. 5.

D'. Children of D, number and sex not known, but some of them known to have had cataract.

G and H. Both developed cataract at from 3 to 5 years of age, operated, and did well. H died, æt. 11.

I, J, and K. Developed cataract rapidly at æt. 2 to 3.

L. Examined and found free from opacity at æt. 3.

M. Commencing cataract, found when examined, æt. 7 months.

CASE 37.—Dor[38] gives the case of a father who had been operated for double cataract at the age of 25. The operations failed, and he became quite blind, but he afterwards married and had 8 children, of whom the 6 eldest had good sight; the 7th

(male) was found by Dor when æt. 7 to have semi-soft degenerated cataracts and nystagmus, and was operated with good result. The 8th child died of infantile diarrhœa. Dor's record of the nature of the father's cataract was, necessarily, incomplete.

CASE 38.—Appenzeller's[21] Case 1 is that of 2 brothers and a sister, in all of whom cataract developed rapidly between 20 and 30 years of age. They were part of a childship of 7, but the places of the cataractous ones and the sexes of remaining 4 are not given.

The parents had good sight, and were not cousins.

CASE 39 (Fig. 17).—In 1884 Arago[23] recorded the following case, the pedigree of which I reproduce in terms of my own "key":—

1*st Branch.*—1. Nuclear cataracts complete, æt. 30; operation success.

2. Medium hard cataracts beginning, æt. 28; operation, æt. 38; success.

3. Soft cataract began, æt. 27; operation, æt. 33; success.

4. Cataracts from childhood, æt. 21; R. shrunken, L. soft; both operated; success.

2*nd Branch.*—5. Cataracts began, æt. 30; very slow; æt. 57, L. medium hard, complete; operation, success.

6. Cataracts began, æt. 20; L. ready, æt. 24; operation, fair success (conditions difficult).

7. Cataract not proved, but was blind, and was operated by a travelling oculist. Died blind.

CASE 40 (Fig. 18).—Sichel (fils)[16] records the following, in which senile cataract "anticipated" through 3 generations, and became finally an affection of early life. The direct continuity, however, was broken :—

1. Operated for double hard cataract in 1845 by Sichel (père). Age at date of operation not stated.

2. Son of 1 ; good eyes.

3. Daughter of 1 ; had double juvenile cataract, which was complete at the age of 18, and operated in 1862 by Sichel (père).

4, 5, and 6. Three cataractous children of No. 2 (who had no cataract). Each was operated in 2nd year of life by Sichel (fils), in 1869, 1872, and 1877 respectively. He calls it "congenital cataract" without further description.

CASE 41.—In another very similar case, Sichel (père) operated for double hard cataract in 1854 upon a man, æt. 62, and in 1865 upon his son, æt. 46, for double semi-soft cataract ; and, finally, Sichel (fils) operated on a son and daughter of the last man (grandchildren of the first patient) at the ages of 13 and 9 for "congenital" cataract that had become complete.

CASE 42.—Females only : 3 generations. Sichel (fils) states that his father operated on a woman and, later, upon two of her daughters, whilst he himself finally operated on a daughter of one of the last patients (maternal granddaughter of the first patient). The ages of these patients are not given.

The following new cases of præsenile and juvenile cataract are given by Daust[45] :—

CASE 43 (Daust's Case 9).—Father, cataract when young ;

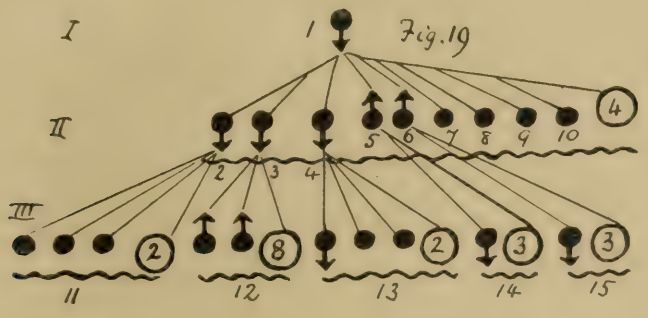
son, punctate cataract diagnosed at 25, but had probably existed from a much earlier age.

CASE 44 (Daust's Case 16).—Shrunken cataract in one eye only of woman aged 34; sight of this eye had never been so good as other; no injury known. Cataract since early youth in 2 sisters of mother, mother herself having good eyes.

Whilst of previously-published cases not hitherto referred to in the present paper, Daust gives the following in abstract:—

CASE 45 (Bock [48], Zehender's Klin. Monatsbl., 1886, p. 227). —Mother, aged 43, a peculiar form of congenital cataract; no evidence of constitutional disease. Daughter, aged 8, double nuclear cataract; and her other children (number not stated) said to have been born with cataract. Mother states she was born with the disease, and that vision has got worse. She has nystagmus, small cornea, deep a.c.s., and tremulous irides. Teeth good in her and her children, and no signs of rickets in any.

CASE 46 (Fig. 19).—Fukala [46] (Internat. klin. Rundschau. Wien, IV, p. 1155):—



1. Double cataract. She had 13 children.

2 to 10. Nine of the 13 who had cataract, and 4 of them transmitted it.

11. Five children of No. 2, of whom 4 had cataract.

12. Ten children of No. 3, of whom 2 (sons) were affected.

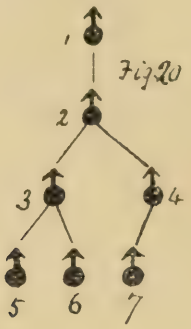
13. Five children of No. 4, 3 of whom were affected, 1 of them (girl) being the patient.

14. Four children of No. 5, 1 of whom (girl) suffered.

15. Four children of No. 6, 1 of whom (also a girl) was affected.

In the whole family the cataract appeared at an early age.

CASE 47 (Fig. 20) (Ziem [47]) :—

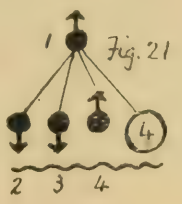


1. Had cataract.
2. Had cataract.
3. Double stellate cataract.
4. Said to have had partial diffuse cataract.

5 and 6. Two sons of 3, aged 19 and 14, both stellate cataract; the one aged 14 was the patient.

7. Man, aged 34, son of 4 and cousin of 5 and 6, also had the same sort of cataract.

CASE 48, Rampoldi [49] (Fig. 21) (Cat. nucleo-corticale in quatre individui della istessa famiglia) :—



1. Operated for cataract. Had 7 children, of whom 4 died with good eyes before 30 years of age, and 3 had cataract, viz.: Nos. 2, 3 and 4.

2. Nucleo-cortical cataract at æt. 38.

3 and 4. Sister and brother of 2, have been operated for cataract.

Case 97, p. 240 (Gjersing's case), should have been placed in this group.

B. CONGENITAL CATARACTS.

This group, as a whole, contains 183 patients, of whom 90 were males and 93 females; besides about 55 others whose sex is not given.

I. We have first a small group in which the cataract is recognised almost at birth or within a few weeks, and is either complete from the beginning or very soon becomes so, and often becomes partially absorbed if not operated upon early, this spontaneous shrinkage leaving a firm central disc or mass completely filling the undilated pupil.

Sporadic cases of this kind are not very rare, but I have found only 9 familial examples, and in 7 of these the cataract was confined to one generation. Two of the cases are my own, 7 are from literature.

The 10 sets of siblings contain 27 cases—male, 13; female 10 (sex unrecorded in 4).

The births of the affected children were successive in 3 instances; in 2 of these certainly, and the 3rd probably they were the 1st and 2nd born. The parents in 4 cases were first cousins.

In 4 others the affected ones were separated by 1 or more children with good eyes; in no one of these 4 was the first-born child known to be cataractous.

In Westhoff's [32] very fully recorded case (Case 51 below), 3 boys, born with complete cataract, were the only survivors of 6 children, the other 3 dying at birth or in early infancy.

In several others there are records of infantile deaths.

The cases certainly produce the impression that we are dealing with some general morbid condition often powerfully affecting the whole offspring and sometimes occurring in both parents. There is no mention of syphilis in any. The cases are as follows:—

Hirschberg [27] has recorded congenital cataract in two pairs of infants of different families. (Cases 49 and 50.)

CASE 49.—Family L. 1. Lina L., æt. 4 months (1874), complete double congenital cataracts. No complications. Both lenses needled, with an interval; child died of "dysentery" before absorption was complete.

2. The next child (sex not stated) was brought with double complete milky cataract a few days after birth; ps. dilated unusually well to atropine. At æt. 9 weeks, when brought for operation, spontaneous absorption had begun, p. having become almost clear on temporal side in L. and nasal side in R. Both needled (November, 1876, and March, 1877) with good result. Child died in early life.

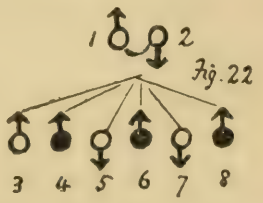
Parents sound.

CASE 50.—Family R. 1. First-born, male (Curt R.); seen, æt. 1½, with both eyes shrunken after unsuccessful operations performed at æt. 6 months at another hospital. Died a few weeks later of diphtheria. History shows that child was born with small eyes and opacity of lenses.

2. Female (Erna) also born with opacity of lenses, and when seen, æt. 6 months, eyes were small (corneal diameter 8 mm.), and ps. not dilatable by atropine. Iridectomy performed, and periphery of lens then found to be clear, but exact character of the central opacity not made out; visual power good.

Parents first cousins, but had good eyes.

CASE 51 (Fig. 22).—By Westhoff[32]:—



1. Father; perfect eyes; good health; carpenter. His father died of apoplexy, with perfect sight. His mother living, æt. 60; perfect sight. No note as to syphilis.

2. Mother; healthy, slight hypermetropia. Her father died, æt. 66, of cancer of stomach; had good sight. Her mother living, æt. 76, with good sight.

3. First child, stillborn.

4. Pupils noticed by parents to look grey soon after birth;

and child, whilst following the movements of a flame, did not try to grasp things presented to it. Seen by W. with complete cataracts, æt. 7 months, but not operated till æt. 1½ year, when needled with success, and at æt. 6 V. with glasses very satisfactory, and fundi n. No fits. General condition very good.

5. Seen by W. soon after birth; no trace of cataract. Died of meningitis, æt. 16 months.

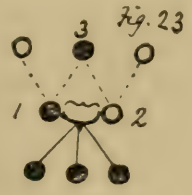
6. Seen by W., æt. a few months with double complete cataract and nystagmus. Needled; good result. No convulsions.

7. Died in convulsions, æt. 4 days. Parents and nurse reported pupils quite black and clear.

8. Seen by W. with complete cataract in one eye, the other being healthy; exact age not stated. Had some fits, otherwise well. No operation.

The 6 children were born between 1887 and 1895, the longest interval, 2½ years, being between Nos. 6 and 7.

Case 52 (Fig. 23).—Gerok[34] has the following instructive examples of "congenital" cataract of unnamed variety:—

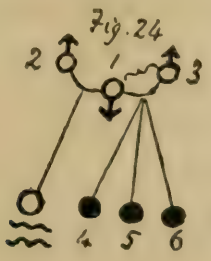


1 and 2. Husband and wife, first cousins; one of them had cataract, but it is not stated whether husband or wife.

They had 3 cataractous children.

A case of cataract (3) had occurred in the generation of siblings, from which 1 and 2 derived their cousinship, but whether 3 was a parent of either 1 or 2 is not stated.

Case 53 (Fig. 24).—Appenzeller's[24] Case 2 is as follows:—



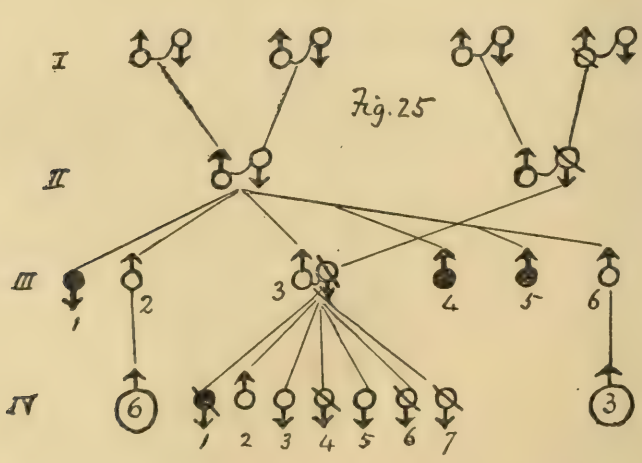
A woman (1) married a man not related by blood (2) and had children, all of whom had good sight. He died, and she then married her first cousin, who also had good eyes (3), and by him had 3 children (4, 5, 6), all of whom were born with double congenital cataract.

No. 4 (sex not stated) was æt. 4 at the date of publication; no particulars of the cataract.

5. Girl, seen by author at æt. 3, had nuclear cataracts with projecting spicules and clear cortex; it is described as peculiar, and was presumably not lamellar. Sex sign omitted in figure.

6. (Sex not stated.) Born 2 years after No. 5; had double cataract, and died at 5 weeks.

No known malformations in the ancestors of either 1 or 3.



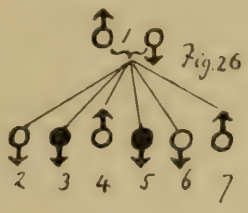
CASE 54 (Fig. 25) (Appenzeller's Case 5).—A girl (IV, No. 1 on pedigree), the first born of 7, was blind at birth, and when examined at 10 years old had dense white cataracts; she also had a malformation of the fingers of both hands. Of the remaining 6 siblings, No. 2 was a boy, and the other 5 girls; none of these had cataract, but Nos. 4, 6, and 7 (girls) had the same malformation of fingers. This malformation (indicated by an oblique line in the diagram) came from the mother's side (Generations I and II). The cataract came through, but not directly from, the father (III, No. 3), 2 of his brothers and 1 sister (III, Nos. 1, 4, and 5) having been born blind (no particulars); and it is to be remarked that the blind sister

(III, No. 1) was the first born of 6. No consanguinity on either side in any generation.

CASE 55 (Appenzeller's Case 7).—A boy of 3 years had cataracts of an indeterminate form and somewhat shrunken; said to have been born with them; no microphthalmos. His father had bad sight from early life, and had been operated successfully for cataract. No consanguinity, and no history of cataract in father, brothers, and sisters, nor in their children.

I have found notes of only 2 cases of my own.

CASE 56 (Fig. 26).—Dearsley (G. B., 1, 168):—



1. Parents, first cousins; good sight. No known history of cataract in previous generations.

2. Æt. 25. One eye blind from corneal ulcer.

3. Edith, æt. 23. Cataracts were seen within 1 day of birth. Operated 5 times between æt. 11 months and 6 years. R. did badly, and shows general opacity of cornea with good p.l. L. did well; p. clear; good fundus reflex; nystagmus; never fits; teeth good.

4. Died, diarrhœa, æt. 13 months.

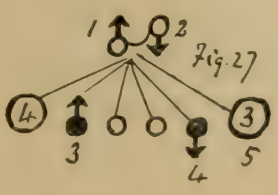
5. Ivy, æt. 18. Dense central cataract. ? Small lamellar, or shrunken lens leaving clear border. Iridectomies, æt. 5; never fits; teeth quite good.

6. Æt. 15; good eyes.

7. Died, æt. 5 months; had fits.

Intelligence good in parents and all the living children.

CASE 57 (Fig. 27).—Kingshott (T.I.P., 1879, p. 179):—



1. Father good sight.

2. Mother good sight; had repeated floodings whilst pregnant with No. 3, but not with No. 4. Died, bronchitis, when No. 5 was æt. about 5 months. Had 11 children.

3. James, 5th child. Cataracts recognised the day after birth. When æt. 3 to 4 years, operated several times. Seen by me, æt. 8 (1879), ps. round and active and a perfectly clear hole in L.; capsule in R. Sees 18 J., with +12 D. Æt. 17 (1888), L., reads tolerably small print with 19 D. No fits. Intelligence good, but head narrow, and boy generally undergrown.

4. Ellen, 8th child. Seen æt. 3 years (1879), with dense yellowish white central cataracts and nystagmus. The opacity consisted of a much shrunken, flattened lens, with nearly clear zone of capsule between it and ciliary processes, through which plenty of light passed. Opacity friable to needle and easily broken up. One eye lost by suppuration. No fits.

5. Three others who died at 6 years, 5 months and birth respectively; their places in the family not stated, except that the one who died at 5 months was the last born of the eleven.

All except 3, 4, 5 on pedigree, healthy.

Case 57*a* was published by Mr. Donald Gunn[52] in 1898, and since then the family has been under the care successively of Mr. Lister and Mr. Parsons at the Hospital for Sick Children. Three generations affected: I, female, cataract became apparent at about 18 years of age; married and bore 7 children (II), of whom Nos. 3, 4, 5, and 6, all males, were "born with cataract." Of the remaining 3 who escaped, 1 was a girl, the sex of the other 2 not stated. No. 3 of Generation II, male with cataract, was operated at age of 16 at Moorfields. He married, and his wife has 4 children (Generation III); there has also been 1 miscarriage; the first-born (girl) has H.As., but otherwise good eyes; 2nd (girl, Maud Bragg) had (in 1897), when 2 years old, shrunken cataracts and nystagmus; she is now (1905) about $10\frac{1}{2}$ years old, and, after repeated needle operations, had V. 6/36 with +8 D.; 3rd (boy), good eyes; 4th (boy, Stanley Bragg), was seen (in 1901) at æt. 1 year, with double cataract (no description), and has undergone several operations with fair success, and is still (1905) under notice.

Other Varieties of Familial Congenital Cataract.

II. Next to lamellar cataract (see below), one of the best marked varieties is the peculiar and apparently rare form called *Axial or Spindle cataract* by the Germans, or, to use Mr. Marcus Gunn's [39] term, *Coralliform cataract*, in which the opacity appears from the history to have been present quite early in life, if not actually at birth, and remains, like the lamellar form, almost stationary, seldom becoming complete.

By far the best example of this sort that I have seen is that of the Betts family (Case 58), in which no less than 30 persons in 4 generations are known to have been affected.

In another, the Ch. family, only 2 siblings were known to be affected.*

Probably some of the cases described by Knies [13] (Case 60) as spindle cataract, and previously under a different title by E. Müller [35], were of this kind; Knies, however, in some of his cases, describes the characters of axial and lamellar cataract associated in various degrees in the same lens. Two of the children in my Case 58 had lamellar cataract, their fathers having coralliform opacity. Moreover, in cases of familial lamellar cataract, atypical forms are occasionally seen (*e.g.*, Galezowski's [21] Cases), some of E. Müller's, and Cases 34, 63, 74, 76, 77, and 79, in which the cataract was not of the same kind in the child as in the parent. Although, therefore, it is necessary for descriptive purposes to keep the axial or coralliform apart from the lamellar cataract, it may, perhaps, be found eventually that both arise from the same, or similar, causes operating at different stages, or over longer and shorter periods of fœtal life.

In this little group, transmission has been continuous in every instance.

The disease attacked successively born siblings often,

* At the June meeting of the Ophthalmological Society Mr. Fisher showed a new case of this form of cataract, referred to below as Case 58*a*; and I have added another, probably of the same nature, seen at St. Thomas's Hospital in 1894 (Case 58*b*).

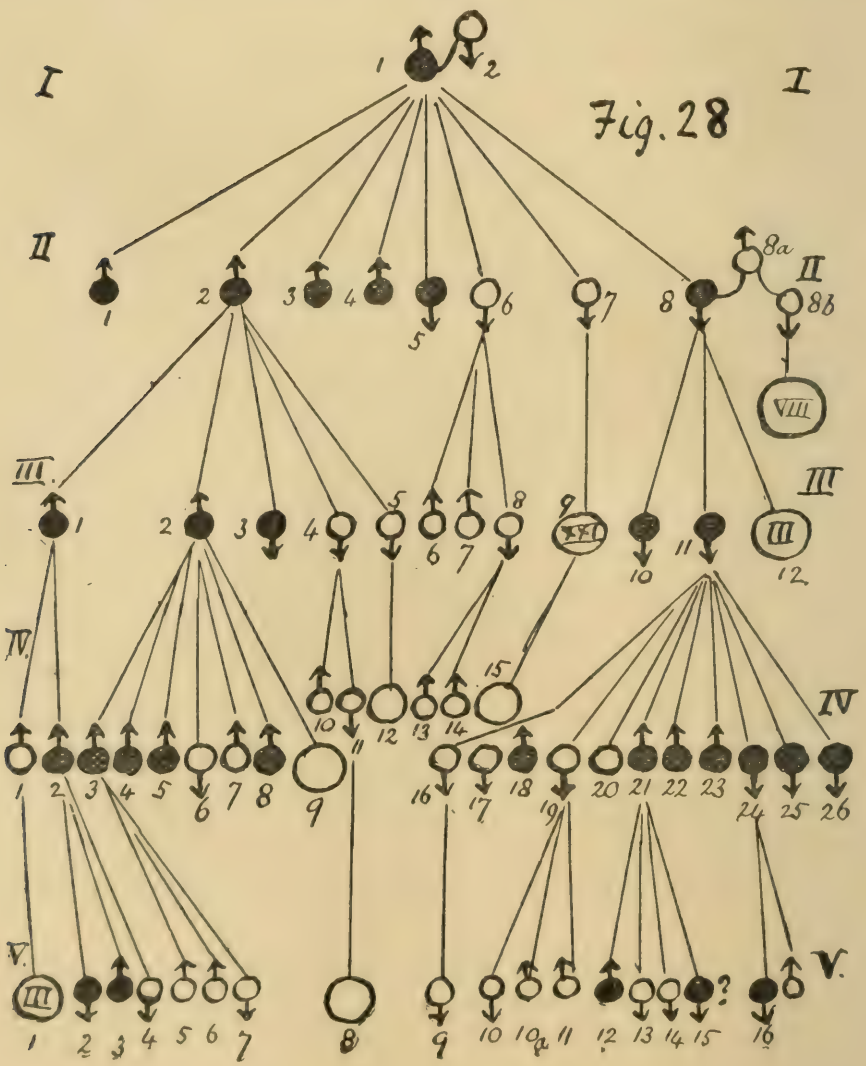
but by no means always. The first-born, whether boy or girl, was usually affected.

The sex prevalence is quite different from anything we have met before : of 46 cases, male, 25 ; female, 21.

Descent in 15 *parentages*, through mother 8 times, through the father 7 times.

Descent to same sex or opposite varied.

Case 58 (Fig. 28).—Betts family. Fig. 28 shows a pedigree of more than 90 persons (probably at least 100), of whom 30 are known to have or have had cataract ; and 19 of these have either



been seen by myself, Mr. Marcus Gunn, or Mr. Walter Sinclair of Ipswich; or are known to have been operated for cataract either at Moorfields or by the late Mr. Bader at Guy's Hospital.

Judging by the history, the cataract must have been present at birth in all cases; it is usually almost stationary, but in two cases some shrinking of the lenses occurred after middle age. With two exceptions, it has presented the same features in every case that has been seen, features very accurately depicted in Mr. Holmes Spicer's drawing of the case (Generation IV, No. 2 in pedigree) published by Mr. Marcus Gunn in vol. xv of the Ophthalmological Society's Transactions (1895), and for which Mr. Gunn has suggested the name "Coralliform." The opacities take the form of dense blunt-ended processes radiating obliquely forwards and outwards (*i.e.*, towards the equator), but not reaching the capsule. Each spoke or process ends peripherally in a sort of trumpet-shaped enlargement or "mouth," not unlike the "mouth" of a madrepore coral. By Knies they have been compared to the sails of a windmill. The intervening parts do not as a rule become quite opaque, even in old age (*cf.* Generation III, No. 11). In two of the cases of Generation V (viz., V2, and one not shown that should lie between 7 and 8)* Mr. Sinclair found ordinary lamellar cataracts, not the coralliform variety. Cholesterine is often present in coralliform cataract.

There has been nothing special in the health or development of this family and no reason to suspect any constitutional disease; no history of convulsions; no deafness. The first known cataractous ancestor was in a small business at the little agricultural town of Hadleigh, in Suffolk. The second generation, and many members, if not all, of the third, also lived or were born there, and some still reside either there or at Ipswich, a few miles off. A large contingent, however, are descended from a mother who left Hadleigh about 40 years ago and has lived near London ever since. There are, I am told, a great many persons named Betts at Hadleigh, some of whom do not recognise any

* Since Fig. 28 was constructed, Mr. Sinclair has discovered that No. 5 of Generation IV has married twice and had 5 children: 1 by the 1st wife, 4 by the 2nd. The one by 1st wife (a boy) had *lamellar* cataracts, and was operated by Mr. Sinclair 10 years ago. The 4 (3 male, 1 female) by 2nd wife have been examined, and all have good eyes. These 5 children should appear between Nos. 7 and 8 in Generation V.

kinship with the cataract clan. Several of the non-cataractous people of this name have married their cousins, but we have not succeeded in tracing any cousin-marriages within the stock known to be affected by cataract, though thorough enquiries have been made.

My acquaintance with this family began in 1883 with the history of Generations I and II, and the cases derived from Generation II, No. 8. For the discovery, quite recently, of those descended from Generation III, Nos. 1 and 2, and for other details, I have to thank my friends, Mr. Edward Howarth, of the Oxford Settlement, Stratford, and Mr. Walter W. Sinclair, Ophthalmic Surgeon to the Ipswich Hospital, who has examined several of them himself. Dr. H. Footman Everett, of Hadleigh, has also most kindly assisted in the search.

A general view of the pedigree shows that the transmission of the cataract was always continuous, *i.e.*, every cataractous child had a cataractous parent; and that of the cataractous ones a decided majority were males (20 males, 11 females), whilst among the 31 with good eyes whose sex is stated 14 were males, 17 females.* Also it is evident that the cataract had no relation to fecundity in the earlier generations. Generation IV, however, has produced comparatively few children (about 30), and of its 6 cases of cataract, 2 have already died: the prospect of transmission to a sixth generation seems therefore to be but small.

Generation I—

A man named Betts, a sack-maker by trade, had bad sight, which his granddaughters (III, 10 and 11) told me was always said by his children (Generation II) to be due to cataract. His wife is known to have had good sight.

Generation II—

1. Robert Betts, cataract, died unmarried.

2. William, cataract. Died about 1887. Five children, of whom the 3 eldest had cataract, the fourth and fifth (daughters) having good eyes.

* In this enumeration the 5 children of IV, 5 (1 boy with cataract, 3 boys and 1 girl with good eyes) not shown on the pedigree, are included.

3, 4 and 5. All had cataract; 3 and 4 married, but left no issue; 5 did not marry.

6. No cataract; had 3 children, all with good eyes.

7. No cataract; said to have had 21 children, all with good eyes.

8. Cataract, Susan B., second wife of Skinner (8*a*), who by his first wife, (8*b*), had 8 children, all with good eyes.

Susan (No. 8) born with bad sight, died at 50, not having had any operation; she had 5 children, of whom the 2 eldest (daughters) have cataract; the 3 youngest died in infancy, and the condition of their eyes is not known.

Generation III—

1. Charles, cataract, operated at Moorfields about 1875, and is still living. Has had 2 children (sons) of whom the younger had *coralliform* cataract (IV, 2); his case was published, with coloured plate, by Marcus Gunn in Oph. Soc. Trans., vol. xv, p. 119, 1895, when patient was 22 years old.

2. John, cataract, operated at Guy's Hospital. Has had 8 or 9 children (order not quite correctly shown on diagram); the first 2 or 3 died in infancy, and the condition of their eyes is not known; then 3 sons with cataract, and a fourth son, the last born (IV, 8), now dead, also had it. The eldest cataractous son (IV, 3) was operated at Moorfields in 1892–3; the other 2 living cataractous sons (IV, 4 and 5) have not been operated upon.

3. Mrs. Glanfield, cataract, operated at Moorfields in 1889 at the age of 51, moderately good result, still living (1905). The cataracts were densely white and appeared to be shrunken; a.cs. deep. Vision had never been good. Had only 1 child, born at seventh month and did not live.

10. Mrs. Warne, cataract, now (1905) aged about 71, and still sees to read with R. eye. R. eye was "needled" at Moorfields when she was 27 and has served her fairly well; when I saw her at about the age of 50 (1884) V. + 14 D = 6/60. L. eye never operated; in 1884 the cataract was complete and shrunken. Has had no children.

11. Mrs. Cross, cataract, R., has been operated; L. typically "coralliform" like IV, 2. Has been seen at intervals since 1884;

last seen January, 1905, æt. 64; L. lens much the same as 20 years ago, but there is now sufficient general haze to prevent illumination of fundus. R. operated repeatedly when aged about 38 without result; now secondary glaucoma. Has had 10 children and one miscarriage (IV, 16 to 26), of whom 7 have cataract.

Generation IV—

A. Children of III, 1—

1. William (of Hadleigh), good eyes; 3 children, all with good eyes.

2. John Adolphus, coralliform cataracts. Case published by Mr. Marcus Gunn. Three children (V, 2, 3, 4), of whom the eldest had *lamellar* cataract and was operated by Mr. Walter Sinclair at Ipswich; she died of diphtheria æt. 7. The second (V, 3) had "white cataract like his father" and died in childhood.

B. Children of III, 2—

3. William (Ipswich), cataracts operated (needled) by Mr. Morton at Moorfields in 1892–93, when patient was aged 17. Result fairly good. Cataract described as "congenital," and before needling the lens showed "opaque pearl-like bodies" towards centre with clear periphery. In 1905 this man has 3 children (V, 5, 6, 7) reported to have good eyes.

4. Arthur, cataract; lives near Manchester; it is not known whether he has been operated or not.

5. James (Ipswich), cataract. Has not been operated. Has 5 children, of whom first-born had lamellar cataract. See footnote to p. 219.

C. Children of III, 11—

16. Cordelia, first-born, and daughter, of III, 11, good eyes. One child, also with good eyes (V 9).

17. Emma, had good eyes, died æt. $3\frac{1}{2}$ years.

18. Hebron, cataract, died æt. $1\frac{1}{2}$ years.

19. Emily (Mrs. Faulkner, notes M. O. P. 1,219), no cataract. At æt. 20 had a large choroidal exudation in R.; had previously had abscess over R. lower jaw leaving depressed scar; lost all her teeth about æt. 18. No evidence of hereditary syphilis,

? tubercle. Seen again January, 1905, æt. 40; nothing fresh. Has had 3 children (V, 10, 10*a*, 11), all of whom have good eyes.

20. Miscarriage.

21. Hebron the 2nd; cataract, both eyes operated æt. 5 or 6. When I saw him in 1883, aged 18, V with + 10 D = 6/18 in each eye; January, 1905, aged about 40, still sees fairly well. Has 4 children (V, 12 to 15), of whom the eldest has cataract (see below); it is believed that the youngest has cataract also.

22. Victor, cataract. One eye operated at æt. 3, inflamed and shrunk, other eye not operated, and with it he still gets on tolerably well at æt. 38 (1905). Married, but no children.

23. Arthur, had cataract and was operated at æt. 2; died æt. 4.

24. Ada, cataract, no operation has been done. In 1893, when she was 24, I found V = 5/60. She has married since then and has 2 children, of which the elder (a girl), now living in Wales, is reported to have cataract (V, 16). Teeth of IV, 24 good, except that the lateral incisors were absent at æt. 14.

25. Kate, cataract, no operation. The condition, which is exactly like the other coralliform cases, was the same in 1905 when she was 32 as when I first saw her about 20 years before. Can see large print; teeth good, no defect of enamel. Unmarried.

26. Arthur, cataract; has not been operated. Married; no children (1905).

Generation V—

A. 2 and 3. See above under IV, 2.

B. Children of IV, 5. See IV, 5, and footnote to p. 219.

C. Children of IV, 21—

12. Sidney Cross, first-born of IV, 21, cataract of the same form as his father (IV, 21) and paternal grandmother (III, 11). I operated on the R. in March, 1896, and January, 1897, at æt. 5, discission followed by extraction. Ten days after the extraction the wound reopened from extensive intraocular hæmorrhage, and the eye was lost; it is believed that he accidentally struck the eye. V. before operation was 6/60. L. not operated, still sees usefully at the age of 15 (1905).

D. Children of IV, 24—

16. Daughter of IV, 24, reported to have cataract.

Case 58*a*.—Mr. Fisher's case, which will be published in the Ophthalmological Society's Transactions, 1905–6, was briefly as follows :—

Miss P. G., nurse, V. always defective; R. cataract needled when æt. 20; "cholesterine came out;" irido-cyclitis and secondary glaucoma. L. typical axial or coralliform cataract, and lately general haze; now æt. 48.

She is youngest of 7; No. 6 (male) also had "congenital" cataracts, and had one eye operated when young without success; the others (Nos. 1 to 5) have good eyes, are all married, and have numerous children, none of whom have cataract. The mother of Miss P. G., who had the 7 children, had cataracts, and had one eye operated with success when æt. 48. P. G.'s father good sight. Three of P. G.'s grandparents known to have had good sight; the fourth she knows nothing about. No consanguinity; father Scotch, mother North of England.

Case 58*b*.—Since the paper was written, I have obtained notes of another case, probably of the same kind.

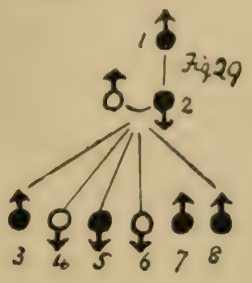
Dobson family (St. Thomas' Hospital, 1884); 3 generations. In Generation I the mother was born with cataracts; one of her daughters (II) was similarly affected. The latter (II) had several children (Generation III), of whom 5 were cataractous, viz., first-born, girl, operated unsuccessfully; 2nd (girl), seen æt. 18, with white anterior polar and nuclear congenital cataract, and 3 others; sex and exact places in the childship not specified. No further particulars.

Case 59.—Miss C., æt. 26 (20, 208, 1890). R.n., Hm. 1, 25, D. L. dense opacity of axial part of lens passing from anterior pole back deeply into lens; there are blunt, or knob-like projections from the axis, like those described in Case 58. Cataract believed to have been present at birth. Enamel of incisors somewhat deficient at cutting edge.

Miss Ruth C., 13 in 1887 (= 16 in 1890) (14,163). L. lens shows a small speck just above posterior pole. Convergent squint usually of L., but almost alternating.

Both eyes emmetropic, and V. normal. History of fits. Teeth show defective enamel.

Case 60 (Fig. 29) (Knies) [133].—Mixed axial and lamellar cataract in three generations.



1. Seen in 1875 with shrunken tremulous cataract; had been blind 21 years.

2. Daughter of No. 1, æt. 36 in 1875. Incomplete *lamellar* cataract. She had 6 children, all carefully examined and described by author; 4 of them had definite cataracts, partly lamellar, partly axial. In the other 2, the eyes, though clear, showed irregular refraction, which was not attributable to the cornea, and was therefore assumed to have its seat in the lens.

3. William, æt. 14½ (in 1875). See Author's Pl., Figs. 1 to 5.

4. Catherine, æt. 13; good eyes.

5. Margarette, æt. 11 (author's Fig. 8).

6. Clara, æt. 9; good eyes.

7. Jacob, æt. 7 (author's Figs., 6*a* and 6*b*).

8. Adam, æt. 3 (author's Figs., 7*a* and 7*b*).

No consanguinity of parents. No history of convulsions in any of the children; teeth perfect in all; no skull deformities nor developmental defects. Intellect bright in all.

III. *Familial Lamellar Cataract.*

Lamellar cataract usually affects only one member of a family or stock. But exceptions to this rule are not very rare, as the examples mentioned below will prove; indeed, according to the authors of some systematic treatises, heredity is common in this form.

I have been able to collect particulars, more or less complete, of 19 families, 6 cases being my own and 13 published by others.

In 8 families only 1 generation was affected, but as

1 of these families had cases in 3 sets of cousins, we have really 11 sets of siblings. They contained 28 cases—13 males, 15 females.

In 6 families 2 generations were affected, yielding in all 25 cases—9 male, 9 female, sex not stated, 7.

In 2 families cases occurred in 3 generations; in all 10 cases—4 male, 6 female.

In 2 families the cataract occurred in 4 generations; in all 12 cases—1 male, 11 females. The great excess of females in this group was due to 1 family, in which all the 7 affected members were female; the cataract is described in these 7 cases as "incomplete lamellar" (Galezowski's [21] case).

The total number of cases amounts to 76—27 male, 42 females, sex not stated 7, or omitting Galezowski's [21], probably atypical case, 27 males, 35 females. The total number of children in 12 of the childships was 67, with 32 cases of cataract.

1. In the 10 families where 2 or more generations suffered, descent was continuous in all.

Only in one or two instances do the records show whether the affected children were successive births or not.

2. Descent was through the mother in 13 generations, through the father in 6.

Descent was to the same sex in 13 generations, to the opposite sex in 8. The mother transmitted to both son and daughter in 2 of this total, but transmission from father to both son and daughter occurred only once.

As to the occurrence of fits, absence of enamel from the permanent incisor and first molar teeth, and defective intellect, the cases of familial lamellar cataract do not appear to differ materially from ordinary ones. In several cases the cataract is noted as being "small" or "very small." On all these points, however, much more material must be collected before any deductions can be made.

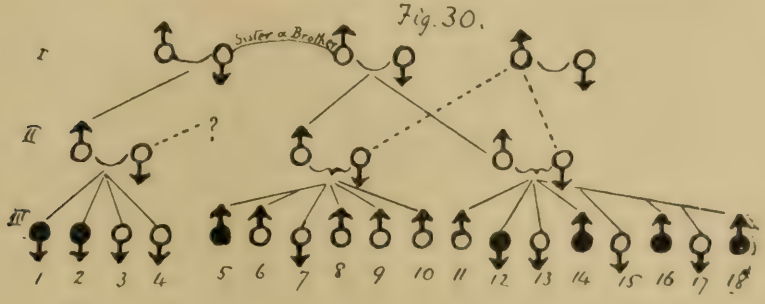
The following are the cases I have collected or seen :—

Case 61.—Saunders [1] (1811) published a case which, from his description and illustration, was undoubtedly typical lamellar cataract in 3 brothers and 1 sister.

In the same place he mentions 3 other familial cases, but, as he gives no description of the opacity, we cannot say positively that these cases were of the lamellar kind.

Case 62 (Fig. 30).—Storbeck's [11] case of familial lamellar cataract is very complicated, and apparently involves consanguinity on both sides, and in more than one generation; I find it impossible to unravel some of the kinships.

It deals with 7 cases of lamellar cataract, in 3 sets of siblings, containing 18 children. All the 18, so far as I can make out, are of the same generation, and all descended from a brother and sister, who had good eyes, and were grandparents to the affected generation. In the youngest subject (Generation III, No. 18), a child, æt. 14 months, the cataract was diffuse in one eye, and typically lamellar in the other. In another, æt. 22 (Generation III, No. 2), one eye showed a double shell of opacity and opalescence of the cortex, whilst the other eye contained a simple, rather small, lamellar capacity. All the others had typical lamellar cataract in both eyes.



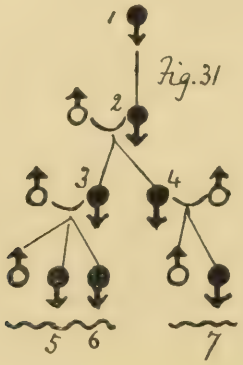
Case 63.—Hirschberg [30] operated on a girl, æt. 15, who had double-layered lamellar cataract of both eyes. Her mother had complete uncomplicated cataract in one eye, and congenital strio-punctate cataract in the other.

Case 64.—In the same paper he narrates the case of a child, æt. 5, with double cataract, whose father, now æt. 30, had suffered from cataract since the fifth year of life, and had been operated upon by von Graefe at the age of 20; whilst a brother

of the father, now æt. 32, who had had iridectomy in 1864 by von Graefe, was now found by H. to have lamellar cataracts.

Case 65.—In a third family, H. found lamellar cataract in both eyes of a child, æt. 1 year, and ascertained that cataract becoming complete at the twentieth year of life had occurred in the 2 previous generations.

Case 66 (Fig. 31).—Galezowski[21]. Cataract in 4 generations, proved to be of lamellar type in the last 2 generations. Females only.



1. Operated for cataract.
2. Operated for cataract.
3. The patient, "incomplete zonular cataract."
4. Sister of No. 3, also patient of Author, with "incomplete zonular cataract."

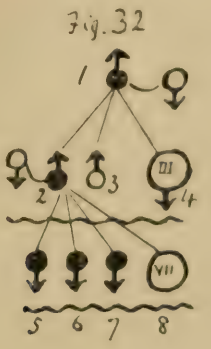
5 and 6. Daughters of No. 3; both with cataracts like their mother's in character.

7. Daughter of No. 4, with cataract resembling her mother's.

Case 67.—In von Arx's[22] dissertation on the Pathology of Lamellar Cataract (1883), giving particulars of 189 cases in Professor Horner's practice, between the years 1865 and 1873, Nos. 100 and 101 were siblings, æt. 37 and 38 respectively, and both giving a history of convulsions. And in his No. 71 (a girl, æt. 8), the father probably had similar cataract.

Case 68.—Davidsen[10] saw lamellar cataract in both eyes of two brothers and a sister, æt. 31, 29, and 24 years respectively. (His cases 1, 2, and 3.)

CASE 69 (Fig. 32).—Hosch[330] (1897) published the following:—



1. Paternal grandfather; an only child. Reclination operation by a travelling oculist, æt. 8; good result in one eye, moderate in other.

2. Adolf W. One of five, but which one not noted. Born (in 1843) with cataracts, diagnosed as lamellar by Horner when æt. 38, at which time artificial pupils were made. Teeth slightly "rachitic."

3. Only brother of No. 2. Died, æt. 4.

4. Three sisters; good eyes. Have between them 14 children, all with good eyes.

5. Sophie W. Born 1872; six toes to each foot. Walked at 12 months. Dentition normal. Cataracts seen by mother, æt. 2 days, by Horner, æt. 6 weeks, and again 6 years, and had not increased; diameter of opaque shell about 4 mm.

6. Elsie W. Born 1882. Cataract seen by mother just after birth. No fits. No rickets. Lamellar cataracts with clear cortex.

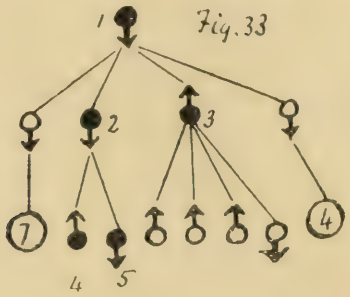
7. Anna W. Born 1885. History and condition same as Nos. 5 and 6. Double shell of lamellar opacity.

8. Seven others, free from cataract.

CASE 70 (Fig. 33).—Horovitz's Case[333], 1903, of Hereditary Lamellar Cataract.

1. Frau D. Lamellar cataract. Diagnosed by Hirschberg in 1888, when patient was aged 50. Had three children, two of whom had cataract.

2. Clara. Diagnosed 1874, æt. 16. No trace of rickets.



3. Eugen. Lamellar cataract diagnosed by Hirschberg in 1898, when patient was aged 35. Had three children, two of whom had cataract.

4. Arthur. Diagnosed 1885, æt. 4; born when Case 2 (his mother) was æt. 23. Rickets of legs; teeth good.

5. Martha. Diagnosed 1891, æt. 6. No traces of rickets, no convulsions.

Case. 71. S. family. Ages as in 1890. Lamellar cataract in second and third members of a childship of six.

1. Mr. C. R. S. (9, 37). 34 in 1890. Em. V. 6/6. Darkish striped choroids. Fair hair and skin.

2. Jane. (17, 81.) 30. Lamellar cataract. Defective intellect. "Mercurial" teeth. Many infantile fits.

3. Florence. (20, 44). 28. The faintest possible degree of lamellar cataract. "Mercurial" teeth.

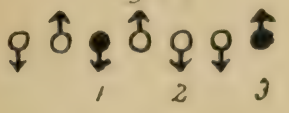
4. Edward. (3, 139). 27. My., 5 D., æt. 16. "Mercurial" teeth. No fits. V. 6/9 corrected; no note of examination of lenses.

5. Hermann. (4, 127). 26. My., 3·5 in R.; Em. in L., æt. 16. Fair hair. No other note.

6. Oscar. (10, 199). 24. My., 2·5 6/6 part, æt. 19. Very fair hair and white skin, but very dark, striped choroids. The mother has light flaxen hair, slight H. and V 6/6.

Case 72 (Fig. 34).—M., sister and brother. (3, 21). In this case Nos. 3 and 7 in a family of seven had small lamellar cataracts, diagnosed in each case at æt. 14. Incisor teeth very good in both patients, and no history of infantile convulsions in either patient:—

Fig 34



1. Third born, Miss M., æt. 14, 1878, when cataracts diagnosed (1890, æt. 24, and in good health).

2. Girl. Died æt. a few weeks.

3. Seventh and last born; Charles, æt. 14, 1890, when cataracts diagnosed.

The other four living and with good sight in 1890.

CASE 73.—M. (17, 60). Family of four sons, daughters not mentioned.

1. Lamellar cataract operated, æt. 13, æt. about 21 when seen by me. Bad teeth and history of convulsions.

2 and 3. No cataract; perfect sight. Good teeth. No convulsions.

4. Cyril M., æt. 16. R., −9 6/24; L., −3 6/18. Lamellar cataracts, faint and rather large, but opacity more dense at posterior pole. Had convulsions, and incisors are deficient in enamel.

CASE 74.—T. O. P., I, 95. Jessie Hawkins, æt. 17. June, 1878.

Very small stationary lamellar cataracts. R. myopia, 10 D., L. about 10 D.; V. about 6/60. Teeth perfect.

Patient is 7th of 8 born; Nos. 1 and 8, both male, said to be short sighted.

Artificial ps. improved V. considerably (6/24). In 1898, M. still 10 d., and V. same.

M. I. P., 1898. Patient (now Mrs. Harrison) brings her son (æt. 12) with diagnosis of "Lamellar Cataracts," but the descriptive notes say "irregular axial opacity from centre of lens to posterior pole." Small myopic crescent. V. 3 months after removal of R. lens and secondary operation + 10 4/60. Enamel of teeth defective. Marked nystagmus. Ps. n. Is second born and only living of three. No. 1 said to have had one eye affected.

CASE 75, Poulton family (T. I. P., 1882. Nos. 334 and 335). —Lamellar cataract in two sisters and a brother.

1. Elizabeth, æt. 13 in 1882 (= 23 in 1892).—Small, very dense lamellar cataracts, smaller than the ordinary undilated ps.; projecting spokes, cortex otherwise clear. Both needled and let out, and did well. Teeth "mercurial." Screaming convulsions in teething, and took many powders. Always delicate.

2. Ethel, æt. 7 in 1882 (= 17 in 1892). Rather dense lamellar cataracts; no note of size. Needled and curetted, evacuation same time as No. 1. Did well. Was treated for fits in infancy.

3. William, æt. 12 in 1892, large, dense, lamellar cataracts, 7 to 8 mm. diameter, with spicules. V. fingers, 6. Shy and nervous. Teeth "mercurial." Was treated as O. P. St. Thomas's for fits, æt. 8 months, and seen by me for eyes, æt. 14 months.

No note of other children nor of parents.

Case 76 (Fig. 35).—Pickett family. (I. P., 1883, No. 250):—

1. Had cataracts.

2. Bad sight as a child, and consequently learnt but little at school. Operated for cataract, æt. 30.

3. Mrs. Pickett, æt. 40 in November, 1883. V. never good enough to allow of reading newspaper print; getting worse, up to 8 years; now (1883) letters of 20 J.; sharply defined anterior and posterior cortical spokes and "indications of clear margin as in lamellar." L. needled and suction; good result. Teeth very bad, most of upper ones gone. No history of fits.

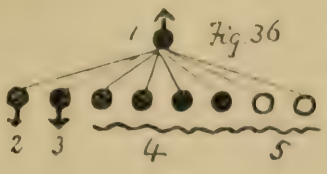
4. Sister of No. 3, V. always defective; operated for cataracts, æt. 16.

5. Louisa P. Daughter of No. 3, æt. 10. Small lamellar cataracts just filling moderately small pupil; no spicules, cortex

quite clear, but rather too visible. Double iridectomy down in. Teeth not mercurial.

Pedigree shows only those who had cataract.

CASE 77 (Fig. 36).—Bresgen [10] :—



1. Aged 58. Cataract R. perinuclear ; L. recently complete ; sight bad in both eyes all his life. Of his 8 children, 6 had cataract.

2. Eldest daughter, æt. 25 ; could never see enough to read or write. Now L. cataract and R. total cataract, which has become rapidly complete during the last year.

3. Second daughter, æt. 23, not able to read or write since æt. 5, owing to lamellar cataracts with central capsular opacities in addition.

4. The four remaining cases, no details.

5. Two who had good eyes.

CASE 78.—E. Müller [85] records in great detail the particulars of a peculiar mixed lamellar and axial cataract in the 3 youngest of 5 sisters, Nos. 1 and 2 having good sight. Those affected were No. 3, æt. 30 at the date of record ; No. 4, æt. 29, and No. 5, æt. 24. The mother, according to the history, was also probably affected.

An excellent half-schematic figure is given of the disposition of the two types of opacity in one of the affected lenses ; this shows that Müller's cases were allied with those published by Knies (Case 60, p. 225).

CASE 79.—Mary Ann Horley (T.O.P. letter), æt. 49, June, 1883. Her son is under care for lamellar cataracts.

Her own sight gradually failing 20 years ; now (1883) 20/O ; R. letters of 18 J., L. letters of 14 J. Cortical cataracts, close beneath anterior capsule, in form of fine dots, and large and small spokes ; all parts of surface of cortex affected, except anterior pole, which is quite free.

Case 79*a*.—Von Hippel (according to Daust [15]) knew of a mother with lamellar cataract, 3 of whose 5 children were similarly affected.

Cases 84 and 85 should be included as lamellar.

Residual Cases.

In cases recorded many years ago, it is often impossible to say what form the cataract took, although in other respects many of these records are very valuable.

Such are, for instance, Maunoir's case, published in 1833; Dyer's in 1846; Armaignac's in 1869; and Baudon's in 1877. In each of these cases 4 generations were attacked.

The two former are fairly complete.

In Maunoir's [4] case 4 generations suffered; 2 members of the 2nd generation transmitted the disease, one of them being unaffected, an instance of discontinuous inheritance.

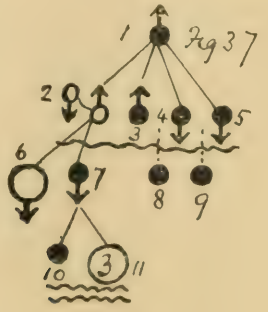
Dyer's [5] case also included 4 generations, and the statement is that only the males suffered. Descent was continuous, and in only one line, and the childships were large.

In Armaignac's [19] case, also of 4 generations, descent was continuous, and in both the 3rd and 4th generation two childships suffered; some of the childships were large.

Baudon's [15] case, of 4 generations, shows the same features as Armaignac's—continuous descent, 2 childships affected in the 3rd generation, and rather numerous children.

Some, *e.g.*, Cases 84 and 85, were almost without doubt lamellar, whilst one (97), Gjersing's remarkable case, should have been placed in the præsenile group, after Case 27.

Case 80 (Maunoir), Fig. 37 :—



Cataract in 4 generations, occurring earlier in the last generation.

1, 3, 4, 8, 9, all operated for cataract. Ages not stated.

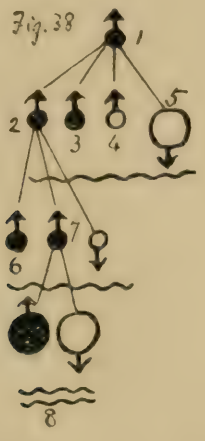
8 and 9 were paternal first cousins of 7, but their sexes and exact parentage not stated.

6. Several sisters of No. 7, good eyes.

7. Cataract formed at æt. 30; no note as to when complete or whether operated. Both her parents were free.

10. One of 4 children of No. 7 was born with cataract; no details.

CASE 81 (Dyer), Fig. 38 :—



A form of congenital or infantile cataract, becoming worse in later life, males only; 4 generations affected.

1. Operated for cataract, æt. 54, and saw well till death some years after. "V. bad from childhood." Had large family, including "several" daughters (Fig. 38, No. 5); none of the daughters affected.

2. Operated for cataract, æt. 62 (1846); had been blind since æt. 40, and V. had always been "misty."

3. Quite blind; age not given.

4. Died young.

5. "Several" daughters, all free.

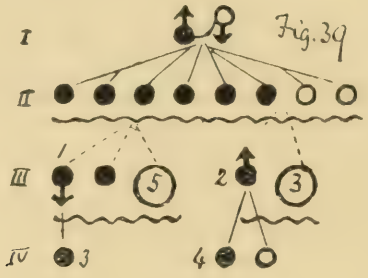
6. Cataract forming (1846); must have been middle-aged then.

7. Apparently in the same state as 6.

8. "Large family" in which all the sons have partial

cataract and all the daughters are free. These siblings seem to have been children at date of record (1846).

The following Case (82, Fig. 39) by Armaignac, in 1881, though incomplete in some particulars, is very striking even as it stands :—



In Generation I the father had cataract; he had 8 children, of whom the 6 eldest had cataract. Nos. 1 and 2 (Generation III) were children of 2 of the cataractous siblings of Generation II, but their parentage is not given more exactly.

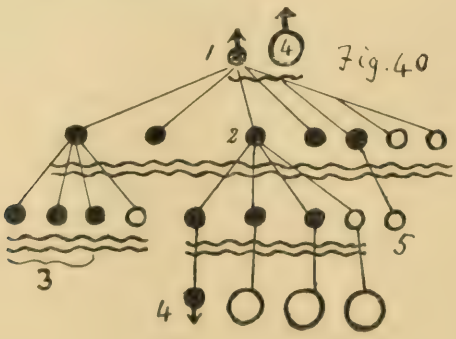
III, 1. Mdlle. K.; never been able to guide herself. Æt. 29, double congenital cataract with normal pupils and good p.l. (implying that cataracts were complete). Microphthalmos, squint, nystagmus. L. extraction, complicated; secondary operation gave some improvement, but no result with glasses.

2. Male—first cousin of No. 1, no details except that he had cataract from birth.

3 and 4. Children of Nos. 1 and 2. In No. 4, the left cataract was complete, and was needled by Author at the age of 5 years with success. The R. was incomplete. Nothing said about operation on No. 3.

Only Nos. 1, 3, and 4 were seen. None of the cases in Generations I and II were seen.

Case 83 (Fig. 40) (Baudon), 1877 :—



Congenital cataract in 4 generations. The kind of cataract not stated.

Information as to sex and order of birth incomplete.

The 1st case (No. 1) was in a man, who had 4 unaffected *brothers*; no mention of sisters.

The last case (No. 4) was a girl, seen by the Author when æt. 2 years, and needled by him. She was a granddaughter of the 3rd affected member of the 2nd generation (No. 2).

3. Three affected children of 3rd generation who were themselves childless at date of the paper.

5. A single child of 4th generation, unaffected.

CASE 84.—Adams[2]. Four siblings, of whom the first-born, a girl (Miss M. P.), had good eyes. The 2nd (girl) had "slate-coloured cataracts, with transparent edges" (doubtless lamellar cataract), when seen at æt. 13. The 3rd (boy), and 4th (girl, æt. 7) had "fluid" congenital cataracts; in the boy the opacity was discovered when he was a month old. All needled with success.

CASE 85.—Appenzeller's[24] Case 6 is that of a father and two sons. The father was born with cataracts, which were operated on about 50 years previously, and who still saw pretty well at date of record (1880), when his age must have been 60, less or more. He had six children, of whom Nos. 3 and 4, both male, were operated for lamellar cataract at the ages of 9 and 6 years respectively, in 1872. Nos. 1, 2, and 5 (males), and No. 6 (female) had good eyes.

No family history of eye disease or congenital anomalies.

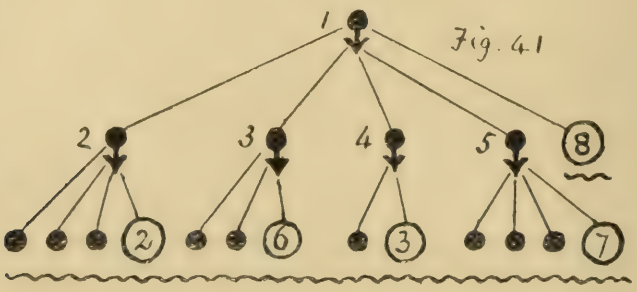
CASE 86.—Adams saw two brothers from Dorsetshire, æt. 20 and 18 respectively, with shrunken congenital cataracts, which he needled with satisfactory results.

CASE 87.—Cahnheim[41] (according to Appenzeller) saw a peculiar posterior cortical cataract in the L. eye of a boy, æt. 6, and in other respects healthy, whose father had been operated for soft cataract, also in the L. eye. The affected eye in the boy was somewhat smaller than its fellow, and its iris darker in colour.

CASE 88.—Mooren[42] (according to Appenzeller) states that he operated for cataract on a mother, and on her infant that was born blind from cataract, with good results.

CASE 89.—Adams operated for "congenital" cataract on two children of a blind Welsh harpist, who was himself born with cataract.

CASE 90 (Fig. 41).—Froebelius[8] gives the following remarkable case:—



1. Had cataract, at what age is not stated. She had twelve children, of whom four (daughters) showed cataract in childhood. Their relative order of birth is correctly shown in the diagram, but the places of the remaining eight children are not given.

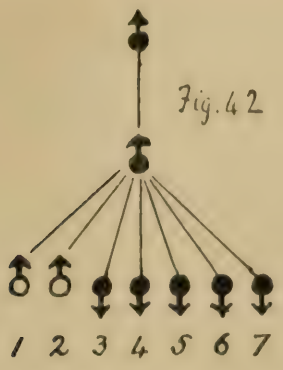
2 to 5. The four daughters who had cataract in childhood. It is especially stated that the husband of No. 2 had good sight, and came from a family free from any history of cataract; no note about the husbands of 3, 4, and 5.

2. Had 5 children, of whom 3 had cataract.
3. „ 8 „ „ 2 „
4. „ 4 „ „ 1 „
5. „ 10 „ „ 3 „

It is stated that the cataract in the 3rd generation came on at an earlier age than in the 2nd generation. Sexes and order of birth of the 3rd generation not given.

CASE 91 (Fig. 42).—Adams records this case, in which 3 generations suffered.

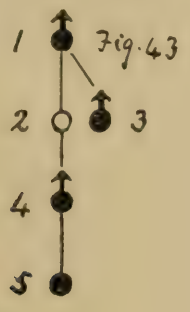
In a family of 7, Nos. 1 and 2 were boys, and had good sight. Nos. 3 to 7, all girls, were all born with double cataract. No. 7 died in infancy, but Nos. 3, 4, 5, and 6 were seen by Adams



at ages varying from 19 to 7. All 4 had nystagmus, and the 3 elder had been previously operated, and showed residual capsular opacities, etc. No. 6, aged 7, had shrunken cataract in the R., and "fluid" cataract in L.; both eyes were needled, and did well.

The mother stated that the children's father (now dead) and grandfather were born blind with the same disease.

CASE 92 (Fig. 43).—Gerok[34] (Case 7) shows "congenital" or "juvenile" cataract in 4 generations, but with a break:



1. "Congenital" cataract.
2. Sex not given; good eyes.
3. Brother of 2; "congenital" cataract.
4. Boy, "juvenile" cataract at age of 8.
5. Sex not given, "juvenile" cataract at 5.

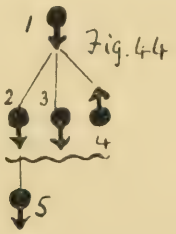
CASE 93.—Bastard[6] (according to Ullmann[20]) gives a case in which 15 cases of cataract occurred between the great grandfather and great grandchildren (4 generations).

A genealogical tree is stated to accompany the original.

Case 94 (Fig. 44).—Lusardi [43]. Observation 3 (p. 33).

In a family named Lantlin, originally at Caen, the mother (Fig. 44, No. 1) has congenital cataracts, but sees well enough to go about alone. Two of her daughters and one son (2, 3, 4 on pedigree) have had cataract from birth, and Lusardi operated on one eye of one of the daughters, when she was 18, with success; she is married, but nothing is said about children. The other cataractous daughter, also married, has a little girl (5 on pedigree) born with cataract.

No details of the cataracts, nor of the other siblings.



Case 95.—Lusardi [43]. Observation 2.

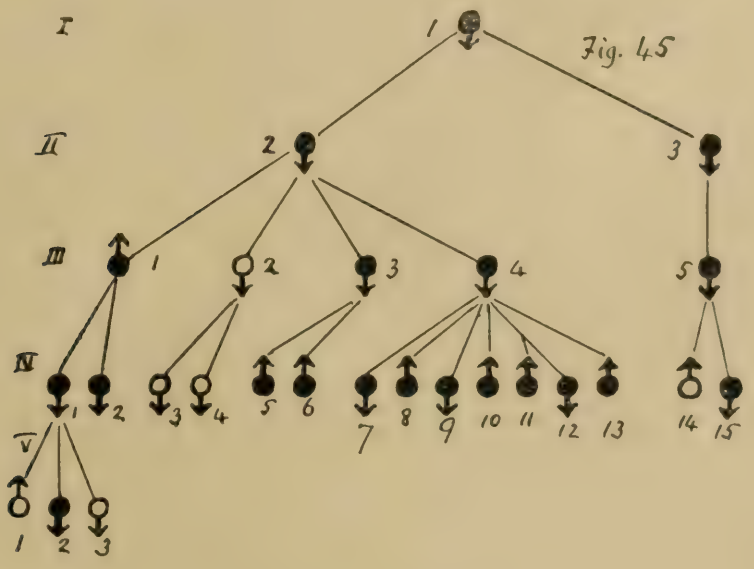
Congenital cataract in 6 of 14 children of parent Decamp (Belgian). The 6 cataractous ones not successive, "*i.e.*, first-born was cataractous, 2nd good eyes, 3rd cataractous, and so on." Two were twins, and of these the 1st had good eyes, the 2nd had cataract, and was still living at date, as also was one of his cataractous brothers. The 1st (of the twins) died æt. 17 months from kick on head by horse. The next birth to the dead one (*i.e.*, to the twins) had good sight, but also died æt. 17 months. Nothing as to sex or kind of cataract.

Case 96.—Lusardi. Observation 4 is that of a man named Wattieaux, who had had cataract since the age of 30; his children, to the number of 5, were born with the same malady. On the same day L. operated on the father and the children, with good result.

Nothing as to sex of children.

Case 97, published by Gjersing [71], really belongs to the præsenile group, and should be read next to Case 27, p. 201. Here no less than 20 cases of cataract occurred in 26 persons in 5 generations; 6 had been operated on at the date of the

paper. The condition does not appear to have been congenital, but it "anticipated" in a very marked degree in the succeeding generations. The family were farmers, and came originally from a small village. The cataract was double in all cases. It began usually as a small opacity at the centre of the lens, radiating streaks appearing later, but not always passing to complete opacity. In one, a child of 8, the cataracts were described as retrograde. Author considers that, though the cataract began earlier in the 4th generation, its rate of progress was decidedly slower than in previous generations. Only one member of the 4th generation out of a total of 15 seems to have been married. The entire family is stated to be very healthy except for the cataract. I find no mention of consanguinity.



Generations I and II—

1. Woman, Nielsen, became blind in old age, almost without doubt owing to cataract. Died in 1840. She had 2 daughters, Nos. 2 and 3 of Generation II, both of whom became blind from hard cataract at the age of 40, and were operated on by the author by reclination, with permanently good result. No. 2 was born in 1801. No. 2, born in 1804, was alive and seeing well at the date of the paper.

Generation III—

Nos. 1 to 4, children of II, 2. In 3 of these sight failed at the age of 30; in the other, the eldest daughter, vision was still good at date of writing.

No. 5, daughter of II, 3, born in 1834, operated by the Author (reclination) with good result.

Generation IV—

Nos. 1 and 2, children of III, 1. Born in 1850 and 1852. Sight failed, about the age of 7, from cataract. No. 1 has 3 children. No. 2, unmarried.

Nos. 3 and 4. Born 1847 and 1852; both good eyes and both unmarried.

Nos. 5 and 6. Born 1848 and 1851. Both had cataract coming on about the age of 7. Both unmarried.

Nos. 7 to 13. Seven children of III, 4, all with cataract coming on about the 7th year. They were born between 1841 and 1863. No. 7 died, aged 9. It is not stated whether any of the others have had children. No. 8, born 1850, was operated by extraction in 1877 for cataract, described by Professor Hansen Grut as irregularly stratiform, with myopia and V corrected 15/200. Moderate success.

Nos. 14 and 15, children of III, 5. No. 14, born 1862, has good eyes. No. 15, born 1869, showed cataract at the age of 7 years; operated on by Professor Hansen Grut in her 12th year. Neither of these two old enough for marriage at date of writing.

Generation V—

Represented by three children of IV, 1, of whom the 2nd (the eldest *girl*), born in 1874, and aged 5 at the date of writing, showed in the R. eye diffuse cataract, in the L. eye a small central white opacity in the lens.

Concluding Remarks.

At the commencement of this paper it was suggested that differences might perhaps be found in regard to inheritance between the two classes, A—acquired or post-natal,

and B—congenital cataract, and throughout the paper various test questions have been put. Though the number of cases is small, especially in the several groups of the congenital class, there do appear to be some important differences between certain groups from the standpoint of heredity; especially between Class A, together with the lamellar group (III) of Class B on the one hand, and the other groups of Class B—the Complete Congenital Cataract (B I), and the Axial or Coralliform variety (B II)—on the other. For example, in Class A and the lamellar group together, we find about three females with hereditary cataract to every two males, whilst in the other two main groups of Class B the males are rather in excess in the comparatively small series available (70 cases). In this connection we may recall the statement on p. 199 that lamellar cataract has been seen in the offspring of a parent with juvenile acquired cataract. There seems also to be a marked difference as to consanguinity between the small group (B I) of complete congenital cataracts and all the rest, for in no less than four out of the ten families of B I the parents were first cousins, whilst in the whole of the remaining cases together there were only three or four known cases of cousin-marriage. But it may be doubted whether consanguinity is really so uncommon as it seems in Class A and groups I and II of Class B, for the fact is noteworthy that some of the families with the longest cataract pedigrees had been settled for long periods in remote country places where consanguineous marriages varying in degree and complexity would be likely to occur though the kinship might often be forgotten. For the present we can only say that consanguinity appears to be rare except in the group of complete congenital cataract.

In some respects, however, there is close similarity between the various groups. For example, the marked preference of the disease in certain stocks for one sex only (either male or female) is seen in several pedigrees of both classes. Again, the rule as to continuity of transmission

holds alike for both classes; and it follows from this that members of a cataract stock who are themselves exempt from cataract transmit good eyes to their descendants, so that in long pedigrees we find "strains" with, and "strains" without, cataract. Lastly, a study of the pedigrees and histories will show that the liability to cataract in a family does not lessen fertility, nor is there, I think, as yet any evidence that the subjects of congenital cataract (except in the little known group B I) are shorter lived than those affected by the senile and præsenile forms of the malady.

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1893. *Fromaget. Gaz. Heb. Scien. Méd. de Bordeaux (quoted by Daust). Lamellar cataract in several generations.

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* Denotes that the original has not been seen.

CAPSULAR COMPLICATIONS AFTER CATARACT EXTRACTION.*

By E. Treacher Collins.

The complications which may arise in connection with the lens capsule after the operation of extraction of cataract may be classified under two headings—

I. Those resulting from its adhesion to the extraction scar.

II. Those resulting from opacity occurring in connection with it.

I. *Complications Resulting from Adhesion of the Lens Capsule to the Extraction Scar.*

Microscopical examination of sections of eyes which have been operated on for extraction of cataract show that an adhesion of the lens capsule to the scar in the cornea, or at the sclero-corneal margin, may be due either to—

(*a*) An entanglement of a portion of the anterior capsule between the lips of the wound; or

(*b*) Agglutination of the capsule to the back of the wound by inflammatory exudate.

(*a*) I have three specimens of eyes lost after extraction of cataract in which the sections show an entanglement of a portion of the anterior capsule in the wound. In two of these it is the distal portion of the divided capsule which is so displaced, and in the other it is the central portion.

All three of these eyes were affected with severe serous irido-cyclitis after the operation, and in two of them sympathetic inflammation was excited in the fellow eye.

The clinical details of these three cases are briefly as follows:—

Case 1.—Joseph B., aged 64, admitted to Moorfields Hospital with senile cataract in February, 1888.

* Read in opening a discussion at a meeting of the British Medical Association, held in Leicester, August, 1905.

An uncomplicated extraction of cataract with iridectomy was performed on the left eye.

The patient suffered from a severe cough after the operation ; there was some iritis.

Six weeks later there was hæmorrhage into the anterior chamber, and the tension became +2.

A paracentesis was performed.

Four days after the paracentesis, and 46 days after the extraction, iritis with keratitis punctata began in the fellow eye.

The increase of tension returned in the eye operated on, and it was excised 48 days after the extraction of the cataract.

Case 2.—Mary K., aged 70, admitted to Moorfields Hospital with senile cataract in September, 1891.

An uncomplicated extraction of cataract with iridectomy performed on the right eye.

Operation followed by iritis, much chemosis and congestion.

Seven weeks after operation keratitis punctata noted and T +2.

Two paracentesises performed at an interval of 10 days.

A week later a needling of capsule, and an attempt made to divide it where it was adherent to the wound.

The iritis continued and the tension remained high.

Five months after the extraction of the cataract the eye was excised.

Case 3.—Harriet S., aged 69, admitted to Moorfields Hospital with senile cataracts in both eyes in December, 1892.

An uncomplicated extraction of cataract with iridectomy was performed on the right eye.

She was re-admitted in February, 1893, and a similar uncomplicated operation was performed on her left eye.

She left the hospital nine days after this second operation, but was re-admitted seven days later with iritis and hypopyon.

Under treatment the hypopyon disappeared, but the eye remained watery and irritable.

Three months later the right eye became inflamed, there was well-marked keratitis punctata and the T. was full. At that time the left eye also had keratitis punctata, and the coloboma was filled with lymph and opaque matter, V. was = p. l. only.

The left eye was excised three months and nine days after the extraction of the cataract from it.

A microscopical examination of the extraction scar in all these three cases shows :—

A thickening of the sclero-corneal tissue in its vicinity, due to the spacing out of the layers of fibrous tissue, and some round cell exudate between them.

An elevation of the conjunctiva overlying it, due to a considerable accumulation of round cells beneath the epithelium.

A prolongation down, in finger-like processes, of the surface epithelium into the scar for some little distance.

A large accumulation of cells between the lips of the wound surrounding the entangled lens capsule. Nearest to the capsule many of these cells are of an epitheloid type ; there are also giant cells of the Langhans type. Outside the zone of epitheloid cells are lymphocytes.

In Case 1 the entangled capsule occupies quite two-thirds of the depth of the wound ; it is much corrugated, and the lips of the wound seem fairly firmly united.

In Cases 2 (Pl. I, Fig. 1) and 3 (Pl. I, Fig. 2) the entangled capsule occupies about half the depth of the wound, and where it is situated the lips are incompletely united. They gape apart, notwithstanding that in the one case five months and in the other more than three months had elapsed since the removal of the cataract.

The inferences which may be drawn from these appearances are as follows :—

That the entangled lens capsule lying between the lips of the wound has acted as a foreign body. It having produced around it just that arrangement of cells which is found around a foreign body implanted in the eye, such as an eye-lash, or the hair of a caterpillar in the affection known as ophthalmia nodosa, viz., a zone of epitheloid cells, some giant cells and lymphocytes.

That the presence of the capsule in the wound has

delayed healing, as shown by the gaping of its lips on the posterior surface, and the downgrowth of epithelium on the anterior surface.

That the delayed closure of the wound increased its liability to become infected by organisms from the conjunctival sac, and that the ensuing irido-cyclitis probably resulted from such infection.

Further, it is highly probable that a tendency to irido-cyclitis was predisposed to in these eyes by the constant drag kept up on the ciliary body through the entangled capsule in the wound.

In Case 1, where it was the central portion of the divided anterior capsule which had become entangled, the ciliary processes at the lower part of the eye were seen to be considerably stretched upwards, and the hæmorrhage, which made its appearance six weeks after the operation, seems to have proceeded from them.

(*b*) The writer has in previous papers* recorded the details of several cases of agglutination of the lens capsule to the posterior surface of the extraction scar by inflammatory exudate. It will suffice, therefore, to give here a summary of the results of his observations on such cases.

Either or both ends of a divided anterior capsule may become agglutinated to the posterior surface of the wound at the sclero-corneal margin after extraction of cataract, or the inflammatory exudate on the posterior surface of the wound may extend between the two lips of the divided anterior capsule and unite the posterior capsule to it.

The agglutination of the capsule to the wound does not delay its healing, as an entanglement in the wound does. The extraction scars which I have examined microscopically, where such agglutination has been present, have been firmly healed without any undue cell accumulation about them.

What it does is to considerably advance the position of the lens capsule from that which it normally occupies in the

* Trans Ophth. Soc. of U. K., vol. x, 1890, p. 108.

eye, and consequently to advance the position of the iris lying in front of the capsule.

In some cases the advance in the iris is sufficient to bring its root into apposition with the posterior surface of the cornea, so obstructing the exit of fluid at the angle of the anterior chamber and giving rise to glaucoma.

The fact that an iridectomy had been done in such cases might at first suggest that glaucoma would be unlikely to occur in them. The writer has found, however, that whenever the peripheral portion of the anterior capsule, or the posterior capsule, is adherent to the extraction scar, the angle of the anterior chamber in the situation of the coloboma has been closed by a small stump of the root of the iris, or by the most anterior of the ciliary processes, which has been held, or drawn forward, by the adherent capsule.

It is in by no means every case where there is an adhesion of the lens capsule to an extraction scar that increase of tension ensues. Clinically, many cases are seen with such adhesions in which a most satisfactory result has been obtained.

The more the advance in the position of the capsule, and secondarily of the iris, the greater the likelihood of the onset of glaucoma.

The more corneal a section is, the greater the advance of the capsule when adherent to it. For this reason, eyes in which the section is made near the sclero-corneal margin are less likely to be affected by glaucoma than those in which it is made in the cornea.

Sometimes in eyes with capsule adherent to the extraction scar, increase of tension does not come on until a subsequent needling operation. In some of these cases the writer has found that a fresh adhesion of capsule to the needle puncture has been produced which has still further advanced its position and brought about a closure of the angle of the anterior chamber by the root of the iris.

In other cases it may be that the congestion of the ciliary processes produced by the drag on them in tearing the capsule just suffices to push forward the root of the iris and cause

apposition of it with the cornea, to which it was previously closely approximated by reason of the adherent capsule.

When the capsule is adherent to the cornea, a fixed point is formed, against which the ciliary muscle has to pull every time it acts.

We know from experience in needling operations how any drag on the ciliary processes at once causes a blush of ciliary injection.

The writer thinks, therefore, that adhesion of the capsule to an extraction scar is a common cause why some eyes remain irritable and refuse to quiet down after operation.

Having described the effects which are liable to be produced by adhesion of the lens capsule to the extraction scar, it will be well next to discuss:

(*a*) How the complication may be avoided.
(*b*) What can be done to remedy the condition when giving rise to trouble?

(*a*) The operation of extraction of cataract without iridectomy is less liable to be followed by adhesion of the lens capsule to the wound than the operation of extraction with iridectomy. In the former the iris usually remains interposed between the divided capsule and the wound.

Adhesion of capsule does sometimes take place when the wound is a corneal one and no iridectomy is performed.

It is by no means very uncommon after the operation of curette evacuation for soft cataract where there has been no iridectomy.

The writer has recorded a case in which a cataract was extracted in its capsule without iridectomy, and where the anterior hyaloid of the vitreous was adherent to the wound. This adhesion drew forwards the iris and caused glaucoma.

In estimating the relative advantages of extraction of cataract with and without iridectomy, the greater liability of capsular adhesions to the wound should always be reckoned as one of the disadvantages of the former.

No method of opening the capsule as yet adopted seems

to exclude the possibility of adhesions, such as have been described, taking place.

If a piece of the anterior capsule be torn out with forceps, no adhesion of it from the corneal side of the wound can form. Entanglements of a peripheral portion of the anterior capsule or agglutination of the posterior capsule could, however, still take place. The writer has sections showing both these conditions from a case in which a portion of the anterior capsule had been removed in this way.

The difficulty in all measures for dealing with entangled capsule is the transparent character of the structure, which renders it impossible sometimes to see if an entanglement is present.

Mr. Swanzy, in his "Handbook on Diseases of the Eye," 7th edition, describes the following method which he employs to prevent incarceration of the capsule: —

"A bent iris-forceps is passed open between the lips of the wound, closed, and drawn gently out again. Frequently a tag of capsule will have been captured by the forceps, and is snipped off with scissors, or it may be that no capsule is caught. The forceps is then similarly inserted at an adjacent part of the wound; and in this manner the wound is searched from end to end for capsule. In about 25 per cent. of the cases a tag of capsule is found present."

Another method employed to prevent incarceration of capsule, and one which the writer generally adopts, is to pass the repositor used for tucking back the iris between the lips of the wound into the anterior chamber, in the situation of the coloboma, making much the same movement as that required for separating the iris from entanglement in the wound.

Simple agglutination of the capsule to the posterior surface of the wound is most likely to occur when there has been some delayed reformation of the anterior chamber which has allowed of their prolonged apposition. Anything, therefore, promoting a rapid closure of the wound tends to prevent agglutination of the capsule to it.

(*b*) The writer has seen a variety of operations performed for the purpose of relieving increase of tension coming on after extraction of cataract.

Sclerotomy, paracentesis, and needling of the capsule almost always fail. Sections of eyes which have been so operated on, which the writer has examined, show that they have not in any way affected the forward traction which the adherent capsule exerts on the iris, and that after all of them the angle of the anterior chamber has remained blocked as before.

An iridectomy, if performed on the opposite side of the eye to that at which the adherent capsule is situated, might open up the angle of the anterior chamber in that situation; it would, however, leave a large and unsightly pupil.

In two cases in which the writer himself has had to deal with this complication, he has attempted to cut through the adhesion of the capsule to the wound by a procedure similar to that described by Mr. Lang for the division of anterior synechiæ of the iris. He has used the same two knives as those employed by Mr. Lang, the one a Knapp's discission knife, the other a similar instrument with a blunt point. With the former he has made a valve-like puncture about the centre of the lower half of the cornea, then having withdrawn the instrument without allowing any aqueous to escape, he has introduced through this puncture the blunt pointed knife, passed it up to one extremity of the coloboma and made its cutting edge sweep across the whole posterior surface of the extraction scar.

In both the cases in which he has performed this operation the increase of tension was permanently reduced.

II. *Complications Resulting from Opacity Occurring in Connection with the Lens Capsule after Extraction of Cataract.*

A microscopical examination of eyes which have had the operation of extraction of cataract performed on them shows

that the membranes left which give rise to opacity may be classified under the following headings:—

(*a*) Retained lens substance.
(*b*) Wrinkling of anterior capsule and new growth of cells lining it.
(*c*) Adventitious fibrous tissue.

(*a*) After the extraction of a cataract any lens substance which is left is at first exposed through the opening made in the capsule to the action of the aqueous humour, but later the opening becomes sealed up by the proliferation of the capsule cells at its margins; any lens substance thus locked up, which if not originally opaque will have become so, is shut off from the dissolving fluid.

A lens, unless extracted in its capsule, is hardly ever removed so completely that some of its peripheral portions are not left which become closed up in this way. It is, of course, only when portions of lens substance are retained in the pupillary area that they give rise to any disturbance of vision, and opacity due to it is seen directly after extraction or within a few days of the operation. Lens substance retained in this way for several years will sometimes have calcareous matter deposited in it.

(*b*) The hyaline lens capsule left after removal of a cataract usually appears thicker than it does in the normal condition. This thickening is not due to any addition to its substance, for it is observed in eyes in which too short a time has elapsed since the removal of the lens to allow of any new growth. It is accounted for by the elastic character of the membrane, which is on the stretch and elongated when it surrounds the lens, but after its removal becomes shortened and thickened.

Though there is a certain amount of shortening, it is not usually sufficient to allow of the anterior part of the capsule lying smoothly in contact with the posterior part over any large area. The anterior part is generally thrown into several folds. These folds by themselves must tend to break

up rays of light and to cause some defect in vision; they are, however, nearly always associated with proliferation of the cells lining the capsule.

The epithelial cells lining the capsule in the region of the nucleated zone, when left after the extraction of a cataract, tend to proliferate, pass round, and then become separated from the capsule, as they do when the lens is intact. They do not, however, as they afterwards enlarge, become flattened out into lens fibres, but form large vesicular cells, sometimes oval, sometimes circular, in shape, this alteration being due to the lessened amount of pressure to which they are exposed.

The cells lining the more central portions of the capsule sometimes also multiply and develop into the same swollen, bladder-like cells, the capsule then being raised into prominences over little groups of them (Pl. II, Fig. 1).

A more frequent result, however, of the proliferation of the cells lining the central portions of the anterior capsule is the lengthening of them out into spindle shapes and into delicate fibres, which form a dense laminated tissue (Pl. II, Fig. 2).

It is with this sort of tissue that the opening left in the capsule after the removal of a cataract becomes sealed up, and with this sort of tissue the spaces left by the rucking of the anterior capsule most frequently become filled.

This tissue exactly resembles that which is met with in anterior polar opacities, which is produced in a similar way, and, like it, varies in its density according to the time which has elapsed since its formation. Occasionally when it has been in existence for a long time hyaline bands are met with between the laminæ.

It is the formation of this sort of tissue which gives rise to the opacity causing deterioration of vision coming on some time after the extraction of a cataract, and the longer it has existed the more fibrous, dense, and tough does it tend to become; consequently the more difficult to cut or tear with a needle.

(*c*) Adventitious fibrous tissue may form after extraction

of cataract as the result of cell exudation in iritis, on the front of the anterior capsule, or between the anterior and posterior capsule, or behind the posterior capsule about the hyaloid of the vitreous as the result of cyclitis. Sometimes a blood clot on the anterior capsule will form a sort of matrix in which fibrous tissue will develop.

In severe cases of iridocyclitis the anterior and posterior capsule may become embedded in fibrous tissue, forming a dense partition between the aqueous and vitreous chambers. It is the contraction of adventitious fibrous tissue on the surface of the anterior capsule, united to the extraction scar, that gives rise to an updrawn pupil after the removal of a cataract.

In an eye in which at the operation for the extraction of a cataract an opening in the lens capsule was made by tearing a piece of it away with forceps, and which, 11 years later, was excised on account of detachment of the retina which, it was thought, might be due to a new growth, sections showed that about two-thirds of the anterior capsule with its lining epithelium had been removed, the posterior capsule without any lining cells being left.

It is obvious that if a portion of the anterior capsule is removed in this way any cortical lens substance which remains in the region from which the piece has been torn cannot become re-enclosed away from the action of the dissolving aqueous humour; so that any opacity occurring after the removal of a cataract due to opaque cortical substance in which capsulotomy was thus performed would only be of temporary duration.

Further, no opacity could form in the region from which the piece had been removed due to the proliferation of the cells lining the anterior capsule.

Occasionally in cataractous lenses cells are met with lining the posterior capsule where normally they are absent. If these were present they would be left, both when the capsule is opened with forceps and with the cystotome. Whether if left freely exposed to the aqueous humour they

would be capable of proliferating and causing some opacity the writer is unable to say, but seeing that lens fibres which normally develop from them are dissolved by the aqueous humour, it would seem improbable.

The removal of a piece of the anterior capsule opposite the pupillary area with forceps would seem, therefore, to be a procedure likely to obviate two of the causes known to give rise to secondary opacities.

For this reason the writer determined in the year 1899 to try removing the anterior capsule with forceps in extracting 100 uncomplicated senile cataracts, and afterwards to compare the results, as regards the number of secondary needling operations required, with 100 cases of a similar character in which he had previously operated by opening the capsule with the cystotome.

In the two sets of cases the operation, except for the manner of opening the capsule, was carried out in a precisely similar way. An incision was made upwards at the sclero-corneal margin, comprising about one-third of its circumference, a conjunctival flap was generally made, and a small iridectomy always.

The use of forceps for the removal of capsule in extraction of cataract seems to have originated with Förster. Mr. John Couper employed forceps for this purpose for many years at the Moorfields Hospital, where the writer, when House Surgeon, had the advantage of watching his dexterous use of them.

The writer commenced by using forceps of the same pattern as those employed by Mr. Couper. These are constructed like a pair of iris forceps, with several teeth projecting and set at an angle on the lower surface of the part which enters the eye.

The arrangement of the teeth is such as to allow of their easily penetrating the capsule and obtaining a good grasp of it. More recently the writer has used forceps with teeth set and arranged in the same way, but smaller in the handle and with a gentle curve like those in use in Vienna.

As a general rule he has considered that a needling operation was required where the vision obtained with glasses after extraction was less than $\frac{6}{18}$ths.

Of the 100 cases operated on by him just prior to March, 1899, in which the capsule was opened by the cystotome, 47 ultimately required a needling, and in seven of these a second needling had to be performed.

Of the first 100 cases operated on since March, 1899, in which a piece of the anterior capsule was removed by forceps, only 15 required subsequent needling, no case required a second needling.

Of the second 100 cases in which a piece of the anterior capsule was removed by forceps, only four required subsequent needling, no case required a second needling, and a period of two years has now elapsed since the last of the second hundred extractions was performed.

The decrease in the number of needlings in the second hundred cases is probably due to an increased experience of the use of the forceps allowing of a successful removal of a large piece of capsule in a larger number of cases.

As the result of his experience the writer thinks it is best, after a small iridectomy has been performed, to introduce the capsule forceps closed to a position opposite the centre of the lens; then to allow the blades to separate to an appropriate extent, and while separate to depress them slightly backwards so that their teeth penetrate the capsule. On the forceps being again closed the capsule can often be seen to ruck up on the surface of the lens, a slight lateral side to side movement should then be made before withdrawing them from the eye. This lateral side to side movement serves to detach the anterior capsule and to prevent withdrawal of the lens in its capsule, which may occur if a pull outwards is at once made.

On two occasions the writer has removed the lens in its capsule by the forceps; in one case its removal in this way was followed by a slight loss of vitreous, in the other case no such loss occurred.

A fear is entertained by many that the use of capsule forceps might cause a displacement of the lens backwards into the vitreous humour. Doubtless such a displacement backwards is possible if an undue amount of pressure is made. The writer has now been using the forceps regularly for five years and no such accident has happened to him. Of the 100 cases in which the capsule was opened with the cystotome prior to March, 1899, vitreous was lost in five. Of the first 100 cases in which the capsule forceps were used in two only was there escape of vitreous, and in the second hundred cases there was escape of vitreous in three. The removal of a piece of the anterior capsule allows the cataract to present and escape from the wound with less pressure on the cornea than when the capsule has been opened with the cystotome. This probably accounts for the smaller percentage of cases in which vitreous was lost where the forceps had been employed.

In the tabulation of his cases another advantage which the writer has found to have resulted from tearing away a portion of the anterior capsule instead of simply lacerating it, is the better vision which the patients afterwards obtain. Out of the 100 cases in which the capsule was opened with the cystotome a record of the subsequent vision has been kept in 80, three cases obtained $V=\frac{6}{6}$ or $\frac{6}{6}$ partly without needling, and five others with a needling; of the three which had $\frac{6}{6}$ without needling, in two the vision two years later had so deteriorated that a needling had to be performed.

Of the first 100 cases in which the capsule was opened with forceps a record of the subsequent vision has been kept in 72, 24 cases obtained $V=\frac{6}{6}$ or $\frac{6}{6}$ partly without needling and two others after needling.

Of the second 100 cases in which the capsule forceps were used a record of the subsequent vision has been kept

Fig. 1.

Fig. 2.

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Fig. 1.

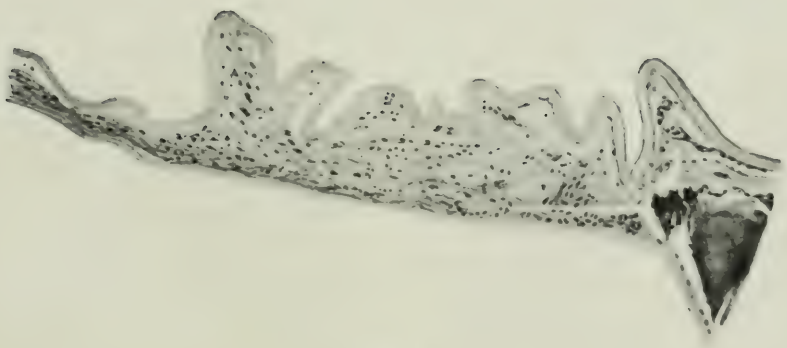

Fig. 2.

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in 73, 27 of these obtained $V=\frac{6}{6}$ or $\frac{6}{6}$ partly without needling and one other with needling.

The writer doubts if by any other procedure for the removal of cataract full vision could be obtained in 25 per cent. of the cases with one operation.

Description of Plates I and II.

Plate I.

For the photographs from which the two figures in this plate have been reproduced the writer is indebted to Mr. E. Collier Green, of Derby.

Fig. 1.—Shows the extraction scar in Case 2. The external portion of the wound is seen to have united. There is some down-growth of the surface epithelium into it shown. The posterior part of the wound gapes widely, and the peripheral portion of the anterior capsule of the lens is seen lying between its lips, surrounded by much cell infiltration.

Fig. 2.—Shows the extraction scar in Case 3. The external portion of the wound has united. The lips of the posterior part are much swollen and infiltrated, they gape widely apart, and the peripheral portion of the anterior capsule of the lens passes forwards between them.

Plate II.

Fig. 1.—Shows the two layers of lens capsule after extraction of cataract, with large bladder-like cells, of subsequent formation, lying between them.

Fig. 2.—Shows the two layers of lens capsule after extraction of cataract, with laminated tissue lying between them, formed by proliferation of the lining epithelium subsequent to the operation.

OBSTRUCTION OF THE CENTRAL ARTERY OF THE RETINA.

By George Coats (Curator).

Cases of obstruction of the central artery of the retina in which a pathological examination has been made are still comparatively rare, and in some instances the descriptions or illustrations have been too meagre to allow of conclusions being drawn on various important points. The total number which I have been able to find in literature is 24. In addition, the diagnosis of "embolism" which v. Graefe instituted from his carefully-observed case, and which was probably correct for that case, has been shown by many writers—notably by Loring, Nettleship, and Priestley Smith—to be hardly tenable for other analogous clinical types. Within recent years, also, several cases have been reported from the purely pathological standpoint tending to diminish the importance of true embolism, and to raise into prominence other factors, such as endarteritis or thrombosis or a combination of these two. This point of view has been especially upheld by Haab and his pupils, and Reimar even goes so far as to say that there is no case on record in which the pathological examination has proved with certainty that a true embolism was the cause of blindness. This statement is much too positive, for there is no reason to doubt that embolism furnishes the best explanation of the pictures and descriptions given by Schweigger, Manz, and Marple. Case 1 reported below, and probably Nettleship's first case, also belong to the same category, and the clinical aspects of Gower's case make this diagnosis likely.

On the other hand, it is not to be denied that, both from the clinical and pathological standpoints, a strong case has been made out for endarteritis as the cause of obstruction in many instances—*e.g.*, in the cases of Elschnig, Wagenmann,

Michel, and Galinowsky. Thrombosis must, no doubt, be reckoned as a very important factor in these cases, but it is not a primary factor, and so far as the pathological evidence goes, does not occur as a causal agent except in association with disease of the vessel wall. A minor exception of no importance to the main question is furnished by a case of Siegrist's, in which blindness of one eye followed upon ligature of all the carotid arteries of the same side, and a coagulum was found in the ophthalmic and central arteries. Such a case, of course, stands in a class by itself, and need not enter into the discussion of the subject of obstruction of the central artery as ordinarily observed clinically.

Theoretically, certain other lesions might cause the same clinical picture, such as retrobulbar neuritis, spasm of the arteries,* hæmorrhage within the optic nerve or in its sheath, and tumours in the same situations; but none of these rests on any pathological evidence, and they will therefore not be further discussed.

In view of the comparative rarity with which such material is obtained for pathological examination, and in view of recent controversies as to the exact nature of the process involved, it seems well to publish and illustrate such cases where possible. The term "embolism" will be used in this paper in its strict meaning as a plug imported into the

* Spasm of the arteries has the support of certain analogies, notably the fine thread-like appearance of the vessels in quinine amaurosis, which has been supposed to be due to this cause. Narrowing of the retinal arteries from spasm has also been described by Raynaud in the disease which goes under his name, but the observation has never been repeated, and has been denied (by Panas) even for the case in which Raynaud described it. (See Raynaud, Arch. générale de Médicin, 1874; Panas, Des Maladies des Yeux. Panas was a colleague of Raynaud's, and examined his ophthalmological cases for him. The whole is quoted in Reimar's paper in Arch. f. Augenheilk, vol. xxxviii, 1899, p. 291.) It is possible that spasm may have played a part in some instances, but almost all the cases which have been pathologically examined have shown changes quite sufficient to account for the symptoms without calling in its aid. Records of spasm of retinal vessels observed ophthalmoscopically are always to be received with caution, as the condition is easily counterfeited when the vessels are badly filled from any cause.

central artery from some other part of the circulatory system, while the more general name "obstruction" will be used to cover all the processes above mentioned, which are usually included under the clinical term "embolism of the central artery."

Case 1 was under the care of Mr. Doyne, to whom I am indebted for the material and the clinical notes.

Caroline M., æt 52, came first to Oxford Eye Hospital in October, 1892. The right eye had been divergent since childhood, and was amblyopic. The vision of the left was less than 6/18. Ophthalmoscopic examination showed cataractous changes in the periphery of both lenses. She was seen again in April, 1897, when vision had sunk in the left to the counting of fingers at four yards, and the lens opacities had much increased. In January, 1900, a preliminary iridectomy was performed on the left eye, from which recovery was perfect except that on one occasion there was slight hyphæma. On July 19th, 1900, a soft and sticky lens was extracted from the left eye. There was slight temperature for a few days afterwards, the lids were a little puffy and the pupil was dilated irregularly, but by August 11th the eye was quite quiet, and with correction she saw 6/18 and J.8. On October 2nd, 1900, a needling was undertaken for some capsular remains in the pupil. The eye remained perfectly quiet after this, but on the evening of October 6th the patient noticed, when the bandage was taken off, that she could see nothing. There had never before been any attacks of temporary blindness. On ophthalmoscopic examination next day the typical picture of obstruction of the central artery was discovered, with an interrupted stream flowing towards the periphery in the branch over the macula. Examination of the heart showed severe endocarditis, double mitral disease, and aortic regurgitation. A history was obtained of rheumatic fever when she was a girl. The urine contained no albumen or sugar.

No useful vision was ever recovered in the affected eye, but for a time she could see a "hole of light the size of a soup-plate" in the temporal side of her field of vision. This, however, was presently lost also, and the eye remained without perception of light. The disc became atrophic, with thread-like vessels. In

addition, a low form of iritis set in, with pain in the eye and brow; the pupil was irregular, and there were numerous posterior synechiæ; the tension was raised and new vessels formed on the anterior surface of the iris, large enough to be seen two feet away, and looking like hæmorrhages. Hyphæma occurred several times. In the hope of giving her a little vision, an extraction was performed on the right, amblyopic, eye, which had by this time also become cataractous, and this was so far successful that she was able to count fingers with it at one metre.

On December 15th, 1903, the patient died, and the left eye was obtained *post-mortem*—about 3 years and 2 months after the occurrence of blindness.

Pathological Examination.—The globe was hardened in formalin, bisected vertically, imbedded in celloidin, and cut in serial sections. The nerve was excised, and cut in transverse serial section from the intraocular surface of the papilla backwards through the lamina cribrosa. Macroscopically the pillars of the iridectomy coloboma and the lens capsule were adherent to the extraction wound. The corneo-iridic angles were occluded, and the disc was deeply cupped.

Microscopic Examination.—The changes in the anterior half of the eye may be briefly summarised. The lips of the corneal wound are separated by new-formed connective tissue containing uveal pigment, and by lens capsule. The latter penetrates right through, and lies close under the conjunctival epithelium. The stump of iris is closely adherent to the back of the cornea, and highly atrophic. There is adhesion of the root of the iris to the cornea also on the opposite side, so that the corneo-iridic angle is completely shut off. The iris itself is condensed and cellular, and its pupillary border is closely bound to the lens remains by a mass of new-formed connective tissue. There is blood in the anterior chamber. Where the lens capsule is not adherent to the corneal wound it has collapsed and enclosed some lens remains, as in a bag; these lens remains are calcareous. There has been some formation of fibres from the lenticular epithelium, as is seen in anterior capsular cataracts. On the anterior surface of the iris there is a layer of cellular tissue containing new-formed blood vessels, but as these are all empty they are not so striking as

might have been expected from the clinical description.* The ciliary body is highly atrophic on the side of the iridectomy, less so on the other. The choroid is much sclerosed and degenerated; there are a few inflammatory patches and some small colloid excrescences. Towards the anterior part there are some adhesions between the choroid and retina.

Retinal and Central Vessels.—For convenience of description, both arteries and veins are followed backwards from the retina up the nerve. The smallest retinal vessels show hyalin degeneration of their walls and obliteration of their lumina. Of the larger, many are collapsed and obliterated, apparently by fibrosis of their walls, but a certain number of them are fairly normal and contain a little blood. On the side of the cup the vessels, both arteries and veins, are highly sclerosed; the minute lumen, however, is lined by a single layer of endothelium—the process is not one of endarteritis, but of fibrosis. Some are completely obliterated, while others contain a few blood corpuscles or a homogeneous coagulum. At the bottom of the cup a single main artery is formed, and almost immediately above this the lumen becomes blocked by the mass shown in Pl. III, fig. 1. This mass is calcareous, and shows a vitreous fracture. In consequence of this it spoiled the knife in cutting the sections, so that it was torn out of some of the succeeding ones, and its exact mode of ending centrally cannot now be studied. It totally fills and over-distends the lumen of the artery where it lies, but it has no connection whatever with the surrounding tissues, which are quite free from any trace of inflammatory reaction. There has therefore been no attempt at organisation. A little slit at one side contains no blood corpuscles, and was probably produced artificially. With high powers the mass is finely granular, and shows no nuclei or remains of blood corpuscles. No endothelium can be detected lining the arterial wall. The entire mass is within the area of the lamina cribrosa. As mentioned above, a similar structure has evidently been torn out of the lumen in the succeeding sections, but just beyond the lamina this ceases to be the case, and the artery is, on the other hand, extremely collapsed and shrunken (Pl. III, fig. 2). Its walls can still be traced, and with

* This condition has been described and figured by Spicer and Parsons in Trans. Ophth. Soc., vol. xxii, p. 306, Plate XXII, fig. 1.

elastic tissue staining, the membrane of Henle can be made out, thrown into zig-zag folds. There is no lumen, but its situation is occupied by an almost homogeneous structure with a few nuclei in it, evidently slightly proliferated endothelium brought together, and adherent in consequence of the collapse of the walls. It has not the appearance of an organised thrombus, since the inflammatory processes necessary to organisation could hardly have left the different layers of the wall so intact and easily recognisable after so long a time. This condition of the artery persists unchanged till the end of the series of sections.

The central vein also shows very profound alterations. At the site of the arterial obstruction the vein is still in two branches, both of which have exceedingly thick walls. In one there seems to be a minute endothelium lined lumen, while the other appears to be entirely blocked. A little farther back this blocked division contains a small cellular organised mass, apparently an organised thrombus. Only a considerable distance up the nerve do these two branches unite to form the single central vein. This has enormously thickened walls, while the lumen is a mere slit (Pl. III, fig. 2). The process has evidently been one of thickening of the connective tissues of the wall—fibrosis—since the lumen is still lined by a single unaltered layer of endothelium. Farther back in the nerve this small lumen becomes entirely obliterated. In no part of the vein are any red blood corpuscles visible.

Retina and Optic Nerve.—The retina shows the changes which have always been found in these cases of obstruction of the central artery, viz., atrophy of the nerve-fibre and ganglion-cell layers, with good preservation of the outer layers which are nourished from the chorio-capillaris. Owing to the long time which has elapsed in the present instance since the occurrence of the obstruction the atrophy is very extreme. Hardly a trace of the nerve fibres is to be detected, while only here and there is a cell to be seen, which is probably not a ganglion cell, since it lacks the characteristic polyhedral form. There is no retinal œdema. The disc is steeply and deeply cupped, and the nerve is in the highest degree atrophic, consisting merely of a shrunken mass of connective tissue without any nerve fibres at all.

Briefly summarised, the pathological conditions found in the case may be stated as follows :—The extraction wound, not firmly healed on account of the intervention of capsule between its edges. Signs of old iritis—posterior synechiæ, new formation of connective tissue with vessels on the anterior surface of the iris, ectropium uveæ, atrophy, adhesion of the root of the iris to the back of the cornea with blocking of the filtration angle. In the central artery, at the level of the lamina cribrosa, a calcareous mass distending the vessel. Extreme collapse and secondary changes in the vessel walls, both in front of and behind this plug, with an organised thrombus in a main branch of the central vein about the same level.

Clinically, the case illustrates a very unusual and disconcerting complication of cataract extraction, but there seems no reason to regard the combination as other than accidental. The changes found in the anterior half of the eye fully account for the occurrence of glaucoma, and, therefore, the case is not analogous to certain others which have been described, in which glaucoma followed upon uncomplicated embolism of the central artery—a sequence of events which will be discussed more fully in connection with the second case.

With regard to the mass in the central artery there seems to be no reason to doubt that it was a true embolus, probably a calcareous nodule from the diseased aortic valves. There cannot have been any high degree of endarteritis in the arteries previous to the block, or they could not have collapsed so completely. The mass fully filled or overdistended the artery where it was situated, yet there was no intimate connection with the vessel wall nor any trace of organisation in spite of the long period during which it had remained there. It can, therefore, hardly have been a nodule of endarteritis or a thrombus. The absence of any organisation is probably to be explained by the fact that the embolus was calcareous when it reached its position, and was, therefore, incapable of cellular invasion. The

microscopical appearances were closely analogous to those found in the cases of Schweigger, Manz, and Marple, and it is noteworthy that in the first two of these cases there was aortic cardiac disease, while in Marple's case, though the condition of the heart is not mentioned, the patient had suffered from rheumatism. In all these cases a true embolism seems to offer the best explanation of the pathological findings, although it may be admitted that the same solution is not suitable or possible for some of the others. In spite, therefore, of recent opinions to the contrary, the occurrence of true embolism of the central artery may be taken as resting on a sound basis of pathological proof.

An interesting clinical point in this case was the preservation for a time of a little vision in the temporal part of the field, although the picture was that of complete obstruction. This is by no means uncommon in recorded cases, apart altogether from the occurrence of unblocked cilio-retinal or macular arteries. The preserved area is almost without exception on the temporal side of the field—on the nasal side of the fovea therefore. I have not met with a perimeter tracing to show its exact position; indeed, perimetry would be difficult to carry out in these cases, since the patient has lost central vision. But an observation of Fischer's is of interest in this connection. By noting on what part of the fundus the ophthalmoscopic image of a small flame fell, he found that the patient had perception of light only in an area of about one-third disc diameter around the papilla. The explanation at once suggests itself that the capillary anastomoses between the ciliary and central vessel systems in this region are capable of keeping up the nutrition of a small zone of retina in the immediate vicinity of the disc.* This raises the much debated question

* Two circles of anastomosis are described in this region: (1) A posterior, by branches from a circle of arteries in the sclera (circulus of Zinn); these have no corresponding veins. (2) An anterior, by branches from the choroidal vessels; these have corresponding veins. In both cases the vessels are little above the size of capillaries. (See Leber, Graefe Saemisch Handbuch.)

as to the amount of collateral circulation which may be established when the main artery is blocked. It is usually taken for granted that this is nil, and, indeed, for practical purposes and so far as the functions of the retina are concerned, it may be admitted that the central artery is an end artery. Yet it is a common observation that arteries which have been thread-like and almost invisible at the time of the occurrence of obstruction, become after a while decidedly better filled or even tolerably well filled. Afterwards, in the course of weeks or months with advancing atrophy of the disc, they again become small and frequently sclerosed.

This well-established clinical fact has given rise to very various conjectures as to its cause. The earliest explanation (Schneller) was that the obstruction was situated in the ophthalmic artery at the point where the central artery was given off, and that it was afterwards carried onwards so as to leave the central artery free to fill up again. While such an occurrence is theoretically possible, it must be admitted that it could only happen very exceptionally, and since the refilling of the arteries is the rule rather than the exception, the hypothesis must be discarded, more especially as no proof has been brought forward in support of it. Another supposition has been that the embolus gets broken up by the blood pressure behind it, and the pieces of it scattered among the retinal arteries, but this is probably impossible without some ophthalmoscopic evidence, evidence which is usually entirely absent.* Or, again, the theory of "incomplete embolism" has been advanced. The plug stops at a part of the artery which it does not completely fill, and the obstruction is made complete by spasm

* In a case of Hirschberg's, however, something of this kind probably really happened. In this instance there were the usual ophthalmoscopic appearances of complete obstruction with very small vessels. The case had been very frequently and carefully watched, and on the morning of the third day was much as at first. On the evening of that day, however, "as by a stroke of magic," all the vessels were normally filled again, except that there was an obstruction some distance out on the inferior temporal artery.

of the arterial wall. Afterwards this spasm relaxes, and the vessel may even become abnormally dilated owing to ischæmic paralysis. Hence a current is re-established. The weakness of this explanation lies in the supposition that a mass whirled along by a tolerably swift current will stop before it is brought up by the narrowness of the vessel lumen or by impinging against a bifurcation. Hence, the theory has been modified by supposing that the plug goes far enough to completely fill the vessel, but that the contraction of the arterial wall which it induces compresses and moulds it to a smaller size, so that when the spasm relaxes again a small lumen is left at the side. It seems probable, however, that secondary thrombosis would prevent re-establishment of the current. These explanations are highly theoretical, and rest on no clear pathological evidence.

Again, it has been supposed that if the obstructing mass were angular and hard—as, for instance, a piece of calcareous cardiac valve—it might lodge in the vessel but still allow some blood to flow past it. But it can hardly be doubted that in this case secondary thrombosis would soon make the obstruction complete. Canalisation of a plastic embolus or of a thrombus is also a possible means of refilling of the retinal arteries. Its occurrence has not been proved in the artery, but I have shown that it may occur in the vein.* In the cases now under consideration, however, the time which elapses before some circulation is re-established is usually much too short to allow of such an explanation. Mr. Nettleship has kindly placed at my disposal some notes of cases observed by him, which show

In spite of this refilling, vision was not greatly improved, the retina having probably been too long anæmic. In this case it seems likely that an embolus or thrombus had obstructed the central artery (probably already narrowed by endarteritis), and that it had suddenly given way at some time of heightened blood pressure, and been carried into the inferior temporal artery.

* R. L. O. H. Rep., vol. xvi, pt. 1, Case 2, p. 83. Another almost exactly similar case has since been published by Sidler-Huguenin, Arch. f. Augenh., November, 1904, p. 27.

that after complete obstruction of the central artery with total loss of sight, some re-establishment of the circulation (as tested by the possibility of producing pulsation in the arteries and by their refilling after emptying) may take place within $2\frac{1}{2}$ hours.

There remains the possibility that the refilling of the vessels is due to the re-establishment of a small collateral circulation. This also cannot be said to be proved for all cases, though there is evidence in its favour. The objection has been raised that if a collateral circulation is formed in this manner, it should go on enlarging until the vessels have reached their normal size, instead of which the vessels after a while again become small and sclerosed. But the amount of collateral circulation which the anastomoses around the nerve head are capable of feeding must be small, since the vessels are of little more than capillary calibre, and are, therefore, probably not capable of indefinite distension, especially on the occurrence of a sudden block. It is a sufficiently well-known pathological principle that a vessel wall tends to adjust itself to the amount of blood flowing through its lumen, not only by partial collapse, but also by thickening. Thus, when the central vein is blocked, not only is the vessel collapsed and with a small lumen higher up the nerve, but its walls are enormously thickened by increase of the connective tissue elements in them. This thickening of the wall decreases as the lumen of the vein gradually becomes better filled by the accession of collaterals. It cannot be a compensatory thickening to meet heightened blood pressure, since the pressure must be greatly lowered just above the block; it must, therefore, simply be due to adjustment of the vein wall to the small quantity of blood in it. The same process of vascular thickening occurs when the central artery is blocked, both in the retinal arteries and in the retinal and central veins, as the present case shows (Pl. III, Fig. 2). This is probably the reason for the final smallness of the vessels, even in those cases which have refilled fairly well after the primary block. The

pathological history of a case might be divided into three stages as follows:—(1) At first the arteries are thread-like from more or less sudden cutting off of the blood stream. (2) Later there is some refilling from the re-establishment of a collateral circulation—we are looking with the ophthalmoscope at a small stream in more or less normal arteries. It is to be remembered that the size of arteries ophthalmoscopically is not necessarily an indication of the amount of blood flowing through them. The velocity of the circulation must also be taken into account, and this cannot be noted unless it falls very far below the normal and indicates itself by visible streaming or beading in the vessels. It is possible, therefore, to have arteries of fair size yet conducting only a comparatively small stream of blood. (3) The last stage is that of the above-mentioned fibrosis of the vessel wall—we are looking with the ophthalmoscope at a small stream in thick-walled arteries, and this corresponds to the final stage of thread-like sclerosed arteries associated with optic atrophy in old cases of obstruction.

It is probable, however, that the freedom of the collateral circulation is subject to individual variation associated with corresponding differences in the clinical course of the case. There are several recorded instances (Schneller, Fischer, Wagenmann, Story) in which, after the picture of complete obstruction, there has been considerable recovery of sight, while on the contrary other cases have never shown any perception of light from the beginning. The usual explanation of these cases with recovery is similar to that given for cases with prodromal obscurations, viz.: there is narrowing of the lumen of the central artery from endarteritis, and if the general blood pressure falls from any cause —not necessarily low enough to cause fainting or cerebral symptoms—it may be insufficient to force the blood past the narrowed part, and the picture of obstruction of the central artery is produced. If, however, within a short time the pressure rises again the blood may force a passage, and

provided that the retina has not been too long anæmic, some vision may still be saved. This is no doubt the explanation of many, perhaps most of these cases, but it is also possible that in some instances the freedom of the collateral circulation, and the rapidity with which it can be established may have something to do with it. The good effects of massage in some cases and its entire inutility in others may also be related to the freedom of the collateral circulation.

The exact position of the block too, as Nettleship has remarked, would probably have considerable influence. If it were extremely far forward, on the inner side of the lamina cribrosa and just at the bifurcation of the vessel, the anastomoses would be shut out from participation because the block would be beyond them; but in this case it might happen that a macular branch was given off from the main artery central to the obstruction, which would preserve some vision by another mechanism similar to what occurs when a cilio-retinal artery is present.* On the other hand if the block lies within or central to the lamina cribrosa the anastomoses of the nerve head have full play. It seems possible that if the block is fairly far forward the superficial portions of these anastomoses will be especially dilated, and this may account for certain cases in which an anastomosis has been visible ophthalmoscopically in the form of fine networks around the papilla. Such networks are sufficiently common in cases of obstruction of veins, but after blocking of the artery they are very rare. I have only been able to find two in the literature, one by Nettleship, and one recently by Gonin. Mr. Nettleship has kindly allowed me to peruse notes and sketches which he has made of a third. These cases furnish strong evidence that some degree of collateral circulation is possible after blocking of the main artery. A

* It is wrong to attribute the preservation of a small triangular field on the temporal side of the disc in every instance to a true cilio-retinal vessel. In many cases this has been the cause (Nettleship, Lang, etc.); but in others the unblocked twig has undoubtedly been a branch of the central artery itself coming off higher than the obstructed portion (Hirschberg, etc.).

case reported by Lawson in which the arteries which were fine and thread-like on the disc suddenly swelled out to their normal size as they crossed its edge, also points in the same direction.

Further, and perhaps even better, proof is furnished by another class of cases—those in which the central artery has been divided with the optic nerve in optico-ciliary neurotomy or for the removal of tumours of the nerve. In these cases although the retina is anæmic at first, the vessels do not remain totally empty, but refill to some extent. A case of Schlodtmann's is of especial importance in this connection. In a case of tumour of the optic nerve the disc had been noted to be atrophic and the vessels of full size. The tumour and optic nerve were excised with preservation of the globe, by resecting the external rectus muscle. An ophthalmoscopic examination undertaken on the evening of the day of operation showed the vessels still of normal calibre, so that it may be supposed that even immediately after the operation they had not been totally empty. Microscopical examination proved that the artery had really been cut, but it had already been obliterated by the growth higher up the nerve, so that the collateral circulation was already in action when the nerve was divided. In another case in which the eyeball was enucleated along with the tumour, the overfilling of the collateral vessels in the nerve was proved microscopically. In these instances two factors were present which are absent in the class of cases which are now under consideration. They differed from embolism cases in that the obstruction was gradual and not sudden, and from cases of endarteritis or thrombosis in that the ciliary vessels, on which the re-establishment of the circulation depended, were probably normal or even distended. A similar case has been observed by Grüning. Restoration of retinal circulation after section has also been shown to occur in rabbits (Wagenmann) and cats (Leber).

Again the central vein is usually regarded as an "end" vein—a vein the obstruction of which is not compensated by

a collateral circulation, and clinically it undoubtedly is so, its blocking being followed by the well-known ophthalmoscopic picture and almost always resulting in permanent damage to the retina. Yet microscopically there is evidence of collateral channels; the vein does not remain collapsed above the obstruction, but a blood-filled lumen is re-established by the accession of small vessels from the trabeculæ. A close analogy may be drawn between what occurs in the vein and what occurs in the artery. In each case on blocking, a collateral circulation is re-established, which however in almost all cases occurs too late and is insufficient in amount to restore function. In certain instances, however, as has been seen, some function *is* restored after complete blocking of the artery, and I have seen a case of typical thrombosis of the central vein in a young person in which all the hæmorrhages cleared up and the vision finally was 6/6.

The little hæmorrhages which are not infrequently seen near the disc somewhat late in obstruction cases are most probably the result of the giving way of capillary vessels under the strain of dilatation in the attempt to re-establish the collateral circulation.

There appears, therefore, to be a considerable body of evidence in favour of the occurrence of a collateral circulation when the main artery is blocked. This evidence may be briefly summarised as follows:—After an obstruction of the main stem of the central artery the vessels do not usually remain empty but refill, with or without some restoration of function. Such refilling is not well explained by flooding onward of the obstruction, or by incomplete blocking by it, or by relaxation of spasm induced by it, and it occurs too soon for canalisation of the plug to play a part. On the other hand the following points make the occurrence of a collateral circulation probable; the occasional preservation of some vision in an area bordering on the disc, the rare presence of visible fine collateral networks, and the not uncommon occurrence of small hæmorrhages in the same

situation, the refilling of the vessels after the division of the artery in the removal of tumours and in optico-ciliary neurotomy, and the analogy of what is known to occur in the veins. Unfortunately, in the present case, owing to the lapse of so long a time since the accident, little evidence can be adduced from the pathological examination. Secondary changes in the vessels, and atrophy of the nerve were much too advanced to allow of any judgment as to whether the collateral vessels had ever been enlarged. It may, however, be said that the block must have been complete and permanent from the first; yet there was visibly some circulation in the retinal vessels shortly after the onset of blindness, and microscopically they contained a little blood.

Case 2.—This case presented itself as a branch obstruction, but the main interest centres in the conditions found in the main stem. I am indebted to Mr. Poulett Wells for the use of this case.

Clinical Notes.—A gentleman, æt. 65, had been complaining of gradual failure of sight in both eyes for some months. Early in October, 1904, the sight of the right eye suddenly became more defective, and he sought advice. The vision of the right eye was 6/24, the pupils active, the tension normal, and the media clear. On ophthalmoscopic examination the superior temporal artery was found to be narrowed, and the blood stream within it was interrupted and showed the characteristic breaking up of the blood column. The circulation in this branch of the artery was distinctly visible in its normal direction, and ceased altogether with the slightest pressure on the globe. The other branches of the retinal artery, beyond showing some thickening of the vessel wall, as evidenced by damming of the venous blood stream where crossed by the arteries, were normal. The veins were normal. Around the macula there were numerous small white retinal patches, and scattered throughout the fundus several small striate hæmorrhages. Examination of the field of vision showed an absolute sector shaped defect down and in, corresponding to the block in the superior temporal artery. In the left eye the vision was also reduced to 6/36, T_n, pupils active, media clear. Ophthalmoscopic examination showed retinal changes similar to the right, but rather more marked. The

arteries presented some sclerosis, but were otherwise normal; the veins were normal. The field of vision was full.

The urine was of high specific gravity, and contained much sugar but no albumen. The heart and lungs were normal.

On November 19th, 1904, sudden violent pain set in in the right eye with vomiting. The patient was seen two days later, when the right eye presented all the signs of an acute glaucoma, with T + 3, and no perception of light. The eye was therefore enucleated next day.

Pathological Examination.—The eye was preserved in formalin, bisected horizontally, and cut in serial sections. The nerve was excised and cut in transverse serial section from its intraocular surface backwards. The anterior chamber is deep, and there is coagulated exudate in the vitreous. The disc is cupped, and beneath it and to its nasal side there is a large exudative patch with a crystalline shimmer, and with hæmorrhage in and around it. Similar but smaller glittering patches are scattered about elsewhere.

Microscopic Examination.—The cornea is normal except for some slight vacuolation of the epithelium. In the anterior chamber there are fibrinous coagula, with a few blood corpuscles and leucocytes. The corneo-iridic angle is blocked, but to a very variable degree in different sections; the blocking is, however, always more pronounced on the nasal side. It is a true adhesion by new formed fibrous tissue, but there has not yet been much atrophy or condensation, and in some cases the extreme angle is free while the iris is adherent to the back of the cornea a little farther forward, a state of things which indicates that the adhesion is of recent origin. In no situation does the adhesion reach quite as far forward as the termination of the membrane of Descemet. The iris tissue generally is loose and uninfiltrated, but the vessels show thickening of their coats and proliferation of their endothelium, changes which in places cause obliteration of the lumen. Towards the root of the iris and also in the anterior part of the ciliary body there are considerable hæmorrhages; these are also present among the spaces of Fontana. The pigment epithelium shows very marked changes on the back of the iris. It is proliferated so as to be in many places several layers thick, while in others it rises into definite small papillæ. In addition, the individual cells are partially

depigmented, so that the dividing line between cell and cell has become more distinct, and it is along these divisions, and especially at the meeting points of several cells that the remaining pigment has become heaped up. The nuclei are often visible, and the dilatator is also seen, but the depigmentation is not sufficient to allow the details of its structure to be clearly made out. These changes cease quite abruptly at the junction of the iris with the ciliary body. Such appearances are well known in the eyes of diabetics; they were first described by Becker, and have been especially studied by Kamocki. There are also some little cysts between the two layers of the pigment epithelium near the root of the iris, and also in the pars plana near the ora serrata. The ciliary body and the choroid are normal.

Retinal and Central Vessels.—Many of the retinal vessels, both arteries and veins, are much diseased, while on the other hand others seem quite normal, and it is noticeable that normal and diseased vessels are often found in close proximity. The process has evidently affected the vessel in a very irregular manner. The smallest peripheral vessels are not infrequently entirely blocked, and sometimes show hyaline degeneration. In the larger vessels the process is clearly one of endothelial proliferation. The connective tissue wall of the vessel is traceable outside; and within it comes a layer of large blown-out cells with nuclei. These have narrowed the lumen in the eccentric manner which is characteristic of endarteritis (Pl. V, Fig. 2). In some cases the cells have a hyaline appearance, and the division between cell and cell is indistinct. In places these changes have caused complete obliteration of the vessel concerned, and this is notably the case with a main upward stem which is probably the one which was seen ophthalmoscopically to be blocked (Pl. V, Fig. 1). Other vessels, however, are markedly affected, which had not been noted ophthalmoscopically to be diseased. (Pl. V, Fig. 2.)

Following the arteries backwards, they show similar changes on the side of the cup, and towards the bottom of it form the main stem of the central artery. This is almost filled by large, ballooned, proliferating endothelial cells, with well defined cell walls. There are, however, a few red blood corpuscles among them, so that the lumen has not been entirely obliterated. The

artery here is much collapsed, but well within the lamina cribrosa this ceases to be the case. The artery suddenly regains its full size, but has its lumen almost completely blocked by endarteritis (Pl. IV, Fig. 1), only a very small cleft-like lumen being left at one side, which contains, however, a few red blood corpuscles. The cells composing this mass are of the same type as before, with large vacuolated bodies and fairly well stained nuclei. In the deepest layers there is a small calcareous nodule, showing the characteristic blue granular staining with hæmatoxylin. For about a quarter of the circumference of the vessel the mass in the lumen is intimately adherent to the wall, but there is no surrounding inflammatory reaction, nor any trace of organisation within it. In this position a small twig is given off from the artery which is also nearly blocked by endothelial proliferation. Staining with elastic tissue stains shows that all these changes are inside the membrane of Henle. The latter does not show its ordinary curly appearance, but is almost straightened out by the distension of the artery, there is no break in its continuity round the vessel. Following the artery backwards up the nerve the calcareous nodule increases in size, and has been ripped out of most of the sections. It also spoiled the edge of the knife, and in making the necessary readjustments after sharpening it again, a little piece of the nerve was unfortunately lost, so that the exact mode of termination of the nodule centrally cannot be described with certainty. It is, however, quite a localised nodule; a short distance above the lamina cribrosa the lumen of the vessel has again become free, of normal size, and blood-filled. The artery now remains perfectly normal for a space, without any thickening of its muscular coat or proliferation of its endothelium. (Pl. IV, Fig. 2.) Some distance up the nerve, however, endarteritis is again met with, narrowing the lumen very considerably in a characteristically eccentric manner. The appearances at this point differ, however, from those seen at the lamina cribrosa in one respect. Here there is considerable proliferation of the elastic tissue which forms the membrane of Henle, so that inside the true lamina there are numerous little curly fibres, as it were, little membranes of Henle. At the lamina, on the other hand, there is nothing of this, the process is purely one of endothelial proliferation, and among the proliferated cells there are no elastic

fibres. This difference, which I have observed in many other cases of endarteritis, is very striking and constant, and corresponds to a difference in the structure of the membrane itself in the two situations. As far as the lamina cribrosa the normal membrane of Henle is a true elastic membrane not resolvable into further details, but in the anterior part of the lamina and within it, it is broken up into a fine feltwork of elastic fibres. It appears that the reaction of the wall of the vessel to the cause of endarteritis is different in these two situations; above the lamina the elastic tissue of the membrane of Henle proliferates along with the endothelium, while within the lamina the elastic tissue fails to do so. Or possibly more correctly, it is the *subendothelial* tissue which proliferates chiefly above the lamina, and which is capable of laying down new membranes, while within the lamina it is the endothelium itself which proliferates, and is incapable of laying down new elastic tissue. At any rate, the fact remains that new formed elastic fibres are not found among the cells which narrow the lumen of retinal arteries in cases of vascular disease, whereas they are found among those which narrow the lumen of the central artery above the lamina.

To return from general questions to the present case however; in following the central vein backwards from the papilla, a single main stem is formed at about the same level as in the case of the artery. In the lamina cribrosa, however, where the obstruction occurs in the artery, this single lumen becomes divided into a number of loculi by connective tissue trabeculæ which traverse it. The vein has thus the appearance of cavernous tissue for a space, and it is difficult to say whether this is to be regarded merely as a peculiarity, or whether there has been a thrombus in it which has organised and canalised. There is no definite vein wall surrounding and enclosing all these loculi, and this favours the first supposition, but on the other hand when the vein has regained a single lumen, as it does some way up the nerve, this lumen is for a time very small and there is considerable round cell infiltration of the wall, facts which would favour the supposition that there had been inflammation and thrombosis (Pl. IV, Fig. 2). The question must be left unsettled. Farther up the nerve the vein receives several large tributaries and becomes of full size again

—much larger than the artery, in fact, which is here narrowed by endarteritis. These relations of artery to vein are preserved unchanged till the end of the series, which does not reach so far as the point of entrance of the vessels into the nerve.

Retina and Nerve.—The chief changes in the retina are found not far from the fovea, although the fovea itself is normal. They consist for the most part of large exudates between the two nuclear layers. These are found in groups in the neighbourhood of the macula, and scattered about irregularly elsewhere; they are either homogeneous or fibrillated, and many vacuoles are present in them. In addition there is œdema of the nerve fibre and ganglion cell layers, so that the limitans interna is raised up here and there in little vesicles. Some hæmorrhages are scattered about, but they are all small and situated in the inner retinal layers, not extending outwards beyond the inner nuclear layer. A few small cysts are present near the ora serrata, and in the same situation there has been a little in-wandering of pigment. The nerve fibre and ganglion cell layers seem to be a little atrophic everywhere, not only in the area supplied by the blocked vessel. The optic nerve is somewhat atrophic generally. No sector of atrophy corresponding to the affected sector of retina can be made out.

Briefly summarised, the pathological changes found in this case were as follows:—Hæmorrhages in the anterior chamber, iris stroma, anterior portion of the ciliary body, and spaces of Fontana. Moderate adhesion of the root of the iris to the back of the cornea without much condensation or atrophy. Vacuolation and loosening of the pigment epithelium strictly confined to the iris and not encroaching at all on the ciliary body. Hæmorrhages and exudative patches in the retina. Narrowing of the lumen of many of the retinal arteries by endothelial proliferation, amounting to complete blocking in the case of the superior temporal. In the main stem at the level of the lamina cribrosa, a localised nodule of endarteritis, almost filling the vessel but leaving a narrow lumen at one side. Farther up the nerve

the artery free for a space and then again much narrowed by endarteritis. The vein cavernous within the lamina cribrosa; farther up the nerve small and with round cell infiltration of its wall, then becoming normal again in size and appearance.

The retinal hæmorrhages and exudates and the advanced vascular disease are to be ascribed chiefly to the diabetes. The association of white patches and hæmorrhages with that disease is, of course, well known clinically, and the occurrence of arteriosclerosis has also been abundantly shown, both clinically and pathologically (Nettleship, Hummelscheim and Leber, etc.). The eye is not the only situation in which the connection is manifest, since arteriosclerosis is certainly a main factor in producing diabetic gangrene of the extremities. In the present instance the branch which actually caused the ophthalmoscopic picture of obstruction is shown in Pl. V, Fig. 1. It showed, as will be noted from the detailed description, neither embolism nor thrombosis, but only an advanced condition of endothelial proliferation which had resulted in its complete blocking. This endothelial proliferation, however, was by no means confined to the branch which had been visibly blocked, but affected to a less degree many of the other retinal arteries which had given very little sign clinically of being diseased.

In addition there was the large nodule in the central artery. It is evident that this must have been of very old standing, since a deposit of calcareous salts had occurred in its deeper layers. As it gradually increased it must have exercised an increasing effect on the intraocular circulation; indeed, one cannot but wonder, considering the little slit-like lumen which alone remains, that ophthalmoscopic evidence of its presence had not been produced long before. The circulation in the retinal arteries must have been greatly slowed, and it is easy to imagine that, since they also were affected with endarteritis, a time came when the deficient stream was unable to force its way through that

one of them which was the most markedly affected. It is unnecessary to call in the aid of thrombosis even, to account for the stoppage of the circulation, although obviously this might readily occur in vessels so diseased, and would produce the same consequences. It seemed not to be present anywhere in the present instance. The ophthalmoscopic appearance of branch obstruction would thus be produced, although the real seat of the mischief lay deeper—in the main stem of the artery.

The following case, although not subjected to pathological examination, may be quoted as being in all probability of the same kind as the foregoing. The patient was under the care of Mr. Treacher Collins, who has kindly permitted me to use it :—

P. S., æt. 52, a bargeman, attended the out-patient department of the R. L. O. Hospital on 16.xi.04, complaining of a slight mistiness before the right eye of five days' duration. V.R. 6/9 ; V.L. 6/6.

Ophthalmoscopic examination showed obstruction of an inframacular branch of the inferior temporal artery in the right eye. The artery was of normal calibre at its origin from the main stem, but a little distance out a faint opacity was seen upon or in it, and beyond this point it became very fine and thread-like. There was a roughly triangular area of retinal opacity corresponding to the distribution of the branch, and a corresponding area of the field of vision was lost—an incomplete sector not reaching to the periphery. Inhalations of amyl nitrite were without effect. The other arteries showed a moderate degree of arteriosclerosis. The fundus of the left eye was normal, except for slight disease of the arteries and banking of the veins where crossed by them.

The patient was a powerfully built apparently healthy man ; there were no cardiac murmurs, and no albumen or sugar was present in the urine. He gave a definite history of having acquired syphilis six months before, and was being treated for it at another hospital. There were some small ulcers on the inner side of his upper lip, some hard painless enlarged glands

in his groins, and a scaly eruption on his head and buttocks. All the palpable arteries were markedly rigid.

A month later he again presented himself with no new complaint. The vision was as before; the vessel formerly obstructed was still thin and thread-like, but the retinal haze had disappeared. There was, however, visible circulation in a small branch of the *superior* temporal artery. The junction of this branch with the main stem could not be traced, but a little bend or knee in the superior temporal indicated where it had come off. Following the artery outwards beyond this gap, there was first a space in which it was extremely small and reduced in places to a fine white line; it then suddenly swelled out, and contained a beaded column of dark venous-looking blood. Just at the spot where it enlarged a very minute branch was given off which at the first moment of examination seemed empty and was just distinguishable. The blood could not exactly be seen flowing in the beaded portion, but the clear areas between the beads altered in position slowly under observation, so that it was evident that some movement was going on in the current. While these vessels were being kept under observation, a dark bead of blood was seen to enter the almost invisible side branch. It very slowly pushed its way outwards, and after a little while lost its connection with the blood in its parent vessel, and slowly disappeared into the periphery, gradually thinning and lengthening as it went. Slight pressure on the globe totally emptied all these vessels, but on relaxing it again they soon refilled, and the same phenomena were repeated, a little more actively for a short time. The vessels on the disc pulsated on slight pressure. No change occurred during an hour or more while he was under observation.

One naturally thought that the circulation was just about to cease in this branch, but this proved not to be so, for on his next visit four days later it was quite re-established. The connection of the branch with the superior temporal artery could be easily seen; the part formerly venous was bright red again, and the little side branch was well filled. There was no beading or visible circulation anywhere.

He did not reappear again for nearly two months, when again his central vision was 6/9, but the ophthalmoscope revealed a

totally new set of phenomena. The main superior temporal artery for about one and a-half disc diameters was of normal diameter. It then suddenly became very thin, being converted into a white streak with just a trace of red in its centre. This lasted for about a disc diameter, and then the artery crossed a large branch of the superior temporal vein, and here there was a hazy white patch completely hiding it, and larger in diameter than the normal artery would have been. The vein was also completely hidden, and showed marked banking peripheral to the crossing. Beyond this the artery was of large size and very dark—quite as dark as the vein ; the blood in it was beaded, and there was no movement at all in the current. Some of its smaller branches were also beaded and without visible circulation. Pressure caused the portion of the artery between the disc and the first constriction to disappear entirely, but had no effect whatever on the dark beaded portion. A sector of the field of vision was lost corresponding to the distribution of the superior temporal artery, and distinct from the area lost on the occasion of the first blocking. The left eye remained normal throughout. Since then the patient has not been seen again.

This is a case of retinal vascular obstruction in which the occurrence of true emboli seems to be out of the question. It is inconceivable that in a man without any demonstrable source for emboli these should have occurred and should have picked out three small vessels in one eye leaving the other eye quite intact. The only possible explanation must be found in a local disease of the arterial system of that one eye. It seems highly probable that this patient had in his right eye a condition similar to that found pathologically in Case 2 reported above, viz., a nodule of endarteritis on the central artery considerably interfering with the circulation in all his retinal branches. These retinal branches themselves were probably similarly diseased though not to a very high degree, since they showed but little change ophthalmoscopically. This, combined with the intraocular pressure, easily produced stoppage of the circulation in individual

branches, but the stoppage was in one instance, at least, capable of being overcome, probably by an improved state of the general circulation. It is very likely that he will some day have an obstruction of his central artery with total blindness, and in that case he will furnish an example of obstruction of the central artery with prodromal obscurations —not quite of the usual type it is true, since between the premonitory attacks vision has not been fully recovered and his fundus has not been normal, conditions which usually obtain in recorded cases with prodromal attacks.

Both these cases are, therefore, of interest with regard to the conditions precursory to the occurrence of total obstruction, and to the question of prodromal obscurations. It has long been considered a point against the diagnosis of true embolism if the patient gives a history of having had previous temporary obscurations of sight before the final attack of blindness, for it is evidently difficult to believe that large numbers of emboli could chance to enter the central artery, or that if they did the obscurations would be temporary and not permanent. More especially is this the case when one eye only is affected over a prolonged period. Nor does thrombosis offer a better solution of the problem, for there is no reason to think that thrombi could appear and disappear in the manner necessary. It is also difficult to believe that embolism is the correct explanation where both eyes are affected (Jessop, Olaf Page, Treacher Collins, etc.), and especially if this occurs simultaneously or nearly so (van Duyse, Knapp Loring, Haase, etc.). In many of these cases also there has been recovery in one eye but not in the other, which seems incompatible with both embolism and thrombosis. The objection seems to have been first stated by Loring, and both he and Nettleship have founded the argument upon it that in these cases there is probably local disease of the vessel wall rendering the retinal circulation liable to temporary interruption from comparatively slight causes—slight lowering of arterial pressure (in sleep for instance), venous stasis from exertion, bending, etc. Case 2

reported above may be looked upon as furnishing the pathological proof of such a supposition. It needs but a glance at Fig. 1, Pl. IV, to see how easily the retinal circulation might be cut off by some such slight cause, and how if this were speedily removed it might be restored again, but if not, how the block might well become permanent with or without thrombosis. Or even if it did not become permanent the retinal elements might be too much damaged to resume their functions when the circulation was restored. Two main factors probably go to the determination of these prodromal attacks, local arterial disease and diminished blood-pressure. In most cases the former of these two is of chief importance and the latter secondary. But in some cases this relation is reversed. Thus in a case of Priestley Smith's the obscurations were associated with fainting turns, due to the pain caused by vaginal douching for an ovaritis. One eye had already become permanently blind during one of these turns, and the douching being continued, repeated obscurations were occurring in the other, associated with faintings. On discontinuing the douchings and removing the offending ovaries both ceased permanently. In this case Priestley Smith's explanation is probably the correct one, that the obscurations were due to cardiac inhibition from the pain, with slowing of the cerebral and ocular circulations, while the permanent blindness of the left was caused by thrombosis of the central artery in that eye. Yet this association of obscurations with other signs of deficient circulation is distinctly exceptional in recorded cases, and it is probable that in most instances, as in the present one, the chief factor is local arterial disease, a cause which Priestley Smith also mentions in the same paper.*

The two cases reported above add to the large mass of

* The only case which I have been able to find in which the fundus was seen *during* one of these prodromal attacks is reported by Wagenmann, Arch. f. Ophth., vol. xliii, 1897, pt. 2, p. 219. He found that the vessels were small and thread-like, and did not pulsate as in ordinary obstruction cases, but quickly refilled with the return of vision. This case ended in an attack which did not pass off, permanent blindness resulting.

evidence already accumulated to show that of all parts of the ocular circulation the part in the immedate vicinity of the lamina cribrosa is that most liable to be affected by vascular disease in any form. This is undoubtedly the case with regard to the vein. In nine cases of thrombosis of the central vein examined by me in which the obstruction was found, it was situated in every one either within the lamina or just above it (central to it). With regard to obstruction of the central artery the fact is no less striking, and this is so whether the obstruction be a true embolus, endarteritis or endarteritis combined with thrombosis. The present cases illustrate the first two of these conditions. From the literature also the cases of Schweigger, Nettleship, Manz, and Marple furnish examples of true embolism in this situation; those of Galinowsky, and (probably) Nuel, Wagenmann, and Schnabel and Sachs' examples of endarteritis; that of Ridley (probably) of thrombosis. It is to be noted that this list includes all the best reported cases, and that in several of the others no obstruction at all was found (Hirschberg, Loring, Popp) probably because the lamina was not cut transversely, while in others again the descriptions are not satisfactory, and it is probable that secondary changes have been taken for primary. It will be evident on looking at Pl. III, Fig. 2, that the changes shown there could easily be taken for the primary obstruction, considering that the eye was obtained $3\frac{1}{2}$ years after the plugging. Indeed, this mistake was very nearly made in that case, for the calcareous mass had broken out of most of the sections and was all but overlooked. The case of Galinowsky is especially interesting, for it is almost exactly the same as Case 2 reported above. Just above the lamina there was a patch of marked endarteritis with a calcareous nodule in it. The case differed only in that the lumen was completely blocked, and clinically there was the picture of complete obstruction and not of branch obstruction as in the present instance.

What is the explanation of the fact that the lamina cribrosa is the seat of election for these various processes?

Many factors probably come into account and act in different degrees in different cases. In the first place the artery becomes narrowed as it passes through the lamina. In a normal eye excised for orbital tumour the central artery measured 145 μ at the lamina cribrosa, 166 μ a millimetre above it. This is a sufficient reason why emboli of a size to enter the central artery at all should become arrested at that point, but, in addition, it furnishes a cause for processes of endarteritis and thrombosis by increasing friction and causing eddies. Then again just beyond the lamina the current meets with increased resistance from two factors—the bifurcation of the main trunk, and the intraocular pressure. These reasons concern the artery alone, but in addition Haab has suggested that the ocular movements have something to do with the occurrence of vascular disease in this situation. The globe is to some extent anchored by the optic nerve, so that during its movements there may be a degree of pulling and dragging just where the nerve is inserted into the eyeball, although this is partly allowed for by the sinuosity of the nerve in its orbital course and by the fact that it is a little longer than the distance from foramen opticum to globe. This factor will act chiefly on the thin-walled and collapsible vein. It is possible also that the lamina cribrosa, which is chiefly composed of elastic tissue, exercises some elastic pressure on the vessels as they pass through it, and that the vessels are, therefore, less capable of compensatory dilatation in this situation. In addition it is certain that the connective tissue around the central vessels is more dense in the region of the lamina cribrosa than elsewhere—as if for protection of the vessels from some outside pressure. (See Pl. IV, Figs. 1 and 2.)

The next question which must engage attention is the connection, if any, between obstruction of the central artery and the subsequent occurrence of glaucoma. In the case of thrombosis of the central vein such a connection has been abundantly proved, and most of the pathological material has been obtained in consequence of this sequence of events.

With regard to obstruction of the artery, on the other hand, while several cases have been reported in which glaucoma followed, the connection is much less certain, and a large proportion of the eyes pathologically examined has been obtained from the *post-mortem* room. In all, glaucoma has been observed some 8 times. It followed within 4 days of the use of a mydriatic in one case (Ridley); a mydriatic had been used in two other cases (two by Nettleship), but whether it had anything to do with the onset of glaucoma or not is doubtful. In another case there were definite signs of iritis (Galinowsky); in Loring's case there were retinal and vitreous hæmorrhages. In a case of Knapp's, which presents many points of resemblance to Case 2 of this paper, the patient suffered from diabetes and an obstruction of the central artery occurred in one eye; later hæmorrhagic iridochoroiditis developed and glaucoma followed probably as a consequence. Thus there are left two (Manz, Marple), or counting Nettleship's 2 cases, 4 cases in which obstruction of the artery and glaucoma occurred in simple association. Is this number higher than might be accounted for by coincidence, or by the obstruction and the glaucoma being due to a common cause, arteriosclerosis, but not dependent the one on the other? In 1891 Fischer had collected over 150 cases of obstruction, and the number of *reported* cases cannot now number less than 200. This would give a percentage of 1 or 2, but in reality such a calculation is of no value whatever, for the clinical picture of obstruction is so well worked out now, that only cases presenting some new or peculiar feature are likely to be reported. On the other hand, cases complicated with glaucoma will probably be published both on account of the rarity of the combination, and because when it occurs it is not unlikely to lead to the obtaining of the eye for pathological examination. It is probable, therefore, that these 8 cases are all or nearly all that have occurred since the clinical characters of obstruction were well known, so that the condition must be one of great rarity—a supposition which accords well with clinical

experience. The combination with glaucoma has not been confined to one type of case; Nettleship's, Manz's and Marple's were probably true emboli, Ridley's thrombosis, and Galinowski's endarteritis.

It will be noted that in the present two cases glaucoma was present. But in the first it had evidently nothing to do with the embolus, but resulted entirely from changes in the anterior part of the eye. In the second case also it was probably not connected with the obstruction of the retinal arteries. There was much hæmorrhage in the root of the iris and among the spaces of Fontana, probably in consequence of vascular disease the result of diabetes, or from the abnormal constitution of the blood from the same cause. The glaucoma was therefore most probably to be referred to interference with the drainage channels. Knapp's case mentioned above is another example of the association of glaucoma with diabetes and hæmorrhagic iridochoroiditis. Hirschberg has also reported a case of glaucoma in a diabetic; it followed upon a hæmorrhagic retinitis. It is difficult to suggest any reason why glaucoma should be caused by a block on the central artery, for such a block will not give rise to any back pressure within the eye or damming back of lymph or blood. There will not probably be any alteration in the chemical constitution of the fluids in the vitreous or anterior chamber, and any explanation depending on changes in the characters of the fluids to be drained off is therefore improbable. In glaucoma following upon thrombosis of the central vein there are many obscure points, but at least there is obstruction of outflow, and some such alteration in the chemical characters of the fluids is conceivable. The evidence, therefore, does not seem at present to be sufficient to decide whether there is any true causal connection between obstruction of the central artery and glaucoma. On the whole the probabilities are against it, but the decision must be left to future research.

Literature.

For convenience of comparison and reference, the cases of obstruction of the central artery which have been subjected to pathological examination have been briefly summarised and set down in tabular form. In order to economise space, the condition of the retina has not been mentioned, for in all the cases in which it has been described it has been the same, viz., atrophy of the nerve fibre and ganglion cell layers with preservation of the outer layers which receive their nourishment from the chorio-capillaris of the choroid. It has been asserted, with probability, on *a priori* grounds that the retinal haze seen soon after the occurrence of the obstruction is not due to œdema as is frequently assumed, but to parenchymatous degeneration or coagulation necrosis of the inner layers of the retina supplied by the central artery No case seems to have been examined early enough to prove this definitely, and œdema has certainly been found in later stages by several authors (Hirschberg, Nettleship, Nuel, Ridley, Manz). The present cases throw no light on the subject. There was indeed œdema of the retina in the second case, but it was clearly connected with the diabetes and not with the obstruction of the artery.

A few explanatory and critical remarks with regard to the cases on the list may be permitted. Schweigger's is the case originally observed by v. Graefe on which the first description of "embolism of the central artery" was founded. From the picture given it seems to be a true case of embolism altogether similar to Case 1 reported above. Sichel's was not a typical case clinically—there was a large macular hæmorrhage—and the significance of the pathological lesion found is also doubtful. Most probably it was a nodule of endarteritis, possibly calcareous, and analogous to Case 2 and Galinowsky's case. In Loring's case no obstruction was found, but it seems probable from the clinical history that one must have been present which was overlooked. The region of the lamina cribrosa was cut longitudinally, not

Author.	Sex and age.	Evidence of vascular or renal disease.	Clinical features.	Pathological examination.
1. Schweigger, Vorles. ü. d. Gebrauch des Augenspiegels, p. 138, and Pl. III, Fig. 10, 1864.	M., ?	Aortic stenosis and regurgitation.	Typical picture. Some vision for a time in temporal field. Eye obtained *post-mortem* 1½ years later.	Rounded mass just above lamina. No organisation or reaction in walls around. Artery filled with thrombus above. (Picture.)
2. Sichel, Arch. de Physiol., vol. iv, p. 83, 1871.	F., 54	Mitral regurgitation. Died with aphasia, etc. No albuminuria.	Sudden loss of vision after a fright. Large hge. in macula and small hges. in periphery. Sclerosis of arteries on disc. Obtained *post-mortem* 14 months later.	In the artery from just behind the lamina for 9 mm. backwards, a mass of round, granular, globular bodies, filling the lumen, and tapering off in both directions. No vein present in the same situation. (Picture.)
3. Loring, Amer. Jl. Med. Sc., vol. lxvii, p. 313, 1874.	F., 62	No cardiac or renal disease. Died of apoplexy following upon phlegmasia dolens 1½ years later.	Retinal and vitreous hges. Cherry spot. Arteries not much reduced. Veins distended. *Glaucoma* 6 weeks later. Excision 2 months from onset.	*No obstruction found.* Central artery and vein nearly empty. Thrombi in choroidal veins. Lamina appeared to contain an excessive amount of fibres and round cells. (No picture.)
4. Nettleship, R. L. O. H. Rep., vol. viii, p. 9, 1874.	M., 54	Aortic and mitral systolic bruits.	Typical picture. Small hges. near temporal side of disc. Some vision for a time in temporal field. *Glaucoma* 3 months later; iridectomy; excision 4 months from onset.	Mass in central artery extending from lamina into retinal arteries and ending in these with a blunt conical point. Probably organising; fibrinous and corpuscular structure, closely adherent to the intima. (Picture.)

5. Priestley Smith, B. M. J., vol. i, p. 452, 1874.	M., 58	Aortic stenosis and regurgitation.	Typical picture. Irregularities in calibre of veins. Obtained *post-mortem* 4 months later.	Artery as a tube no longer in existence, but its position indicated by a circular mass of concentrically arranged fibrous tissue. (No picture.)
6. Schmidt-Rimpler, Arch. f. Ophth., vol. xxii, pt. 2, p. 287, 1874.	?	Hypertrophy of heart and atheroma of aortic valves. R. hemiparesis 2 months before onset of blindness.	Blindness coming on during night. Exophthalmos and chemosis. Later, iritis and some retinal hges. Obtained *post-mortem* 10 months after onset.	Yellow mass mostly hyaline, completely filling lumen of artery some distance above lamina; a few nuclei in it and ? some vessels. Retinal vessels thickened, and some of them on papilla plugged. (Picture.)
7. Nettleship and Watson, R. L. O. H. Rep., vol. viii, p. 251, 1875.	F., 62	"Cardiac murmur."	Blindness with pain in head and limitation of movement of eyeball; no protrusion. *Glaucoma* 2 months later; iridectomy; enucleation 6 months from onset.	At lamina, and within it, artery contained a fibrous-looking material, mixed with molecular substance containing scattered corpuscles. Vein probably thrombosed. (Picture.)
8. Gowers, Lancet, vol. ii, p. 794, 1875.	M., 30	Mitral systolic murmur and dilated heart. No albumen. R. hemiplegia proved *post-mortem* to be due to embolism of middle cerebral artery.	Typical picture L. discovered 5 days after onset of R. hemiplegia. Arteries larger in periphery than on disc. Obtained *post-mortem* 3 months later.	Many minute granular masses in central artery, largest ½ inch above lamina. Similar masses in vessels on disc. (Picture.)

Author.	Sex and age.	Evidence of vascular or renal disease.	Clinical features.	Pathological examination.
9. Popp, Inaug. Diss. Regensburg (quoted in Manz), 1875.	F., 60	"Disease of the heart." Cerebral vessels calcareous.	Obtained *post-mortem* 3 years after onset of blindness.	*No obstruction found.* Retinal and central vessels normal.
10. Nettleship and Lawford, Trans. Ophth. Soc., vol. ii, p. 52, 1882.	M., 63	Heart normal. Glycosuria and albuminuria. Had been treated for "diabetes" when 18 years old.	Diabetic retinitis both, with picture of obstruction of central artery, L. Obstruction seemed to be visible on disc. Died of diabetic gangrene. Obtained *post-mortem.*	Artery thickened. Coats puckered, and lumen almost obliterated. No embolus found. Hyaline thickening of choroidal and some retinal vessels. Diabetic changes in retina, and great atrophy of nerve fibre layer. (No pictures.)
11. Hirschberg, Centralbl. f. prakt. Augenh., p. 1, 1884.	M., 45	Aortic stenosis and regurgitation. No albuminuria.	Typical picture. Prodromal obscurations 4 weeks before. Some small hges. at edge of disc. Obtained *post-mortem* 5½ months after onset.	*No obstruction found.* Retinal and central vessels normal. (Pictures.)
12. Schnabel and Sachs, Arch. f. Augenh., vol. xv, p. 11, 1885.	M., 33	Aortic stenosis and regurgitation. Mitral regurgitation. Slight albuminuria.	Typical picture L. 24 hours later arteries well filled, and showing beading and visible circulation in normal direction. 5 days later temporary obscu-	Obstruction at lamina partially occluding lumen, but with small blood-filled lumen at one side. Covered with endothelium. Similar structure in inferior main temporal artery, and other

			rations R.; recovered and remained normal till death 3 months later. Obtained *post-mortem*.	retinal arteries thickened. (No pictures.)
13. MANZ, Festschrift f. v. Helmholtz, p. 1, 1891.	F., 65	Aortic disease. Albuminuria.	Typical picture. V = fingers at ½ metre temporally only. Attacks of *glaucoma* 10 months and 1 year later. Death a little more than 1 year later. Obtained *post-mortem*.	Embolus at anterior part of lamina just at bifurcation of vessels; probably calcareous; no definite structure. Artery dilated and thrombosed farther up nerve; vein collapsed. A.C. deep. ∢'s blocked. Blood in root of iris and spaces of Fontana. (Picture.)
14. ELSCHNIG, Arch. f. Augenh., vol. xxiv, p. 65, 1892.	F., 50	Cardiac hypertrophy, sounds normal. Albuminuria. R. hemiplegia. *Post-mortem;* endarteritis of cerebral vessels and thrombosis of middle cerebral. Cardiac valves normal.	Typical picture L. discovered 4 days after onset of hemiplegia. Died 7 weeks later. Obtained *post-mortem*.	Obstruction in both main branches of central artery not completely blocking either. Lumen narrowed eccentrically and clothed with endothelium. Only slight endarteritis in central artery itself. (Pictures.)
15. WAGENMANN, Arch. f. Ophth., vol. xl, pt. 3, p. 221, 1894.	F., 45	Mitral insufficiency and stenosis. Granular kidneys.	Typical picture seen 5 days after blindness. A few small hges. near disc. Arteries remained very small, but pulsation returned. No p.l. at any time. Obtained *post-mortem* 12¼ months later.	Obstruction close behind lamina. Cellular mass with fine fibrils, fatty cells, cholestearin, and giant cells, leaving a minute endothelium-lined lumen partly at one side, partly within the mass. Much endothelial proliferation. Retinal arteries showed endothelial proliferation, and some were occluded. (Pictures.)

Author.	Sex and age.	Evidence of vascular or renal disease.	Clinical features.	Pathological examination.
16. Marple, New York Eye and Ear Inf. Rep., vol. iii, p. 1, 1895.	F., 56	?	Typical picture. Returned in 7 weeks with *glaucoma* apparently of some duration. Enucleated.	Embolus $\frac{1}{4}$ mm. by $\frac{1}{6}$ mm. immediately above lamina. Little structure, and probably calcareous; vessel dilated at this spot; contains corpuscles both in front of it and behind. Artery makes a sharp bend just peripheral to the obstruction. (Pictures.)
17. Ridley, R. L. O. H. Rep., vol. xiv, p. 264, 1895.	M., 57	Occasional cardiac irregularity; no murmurs; no albuminuria.	First seen 2 months after loss of vision. Vitreous opacity. All vessels much contracted except sup. temp. vein. H. and C. instilled for examination; eserin before he left. Returned in 4 days, having had pain since former visit. *Glaucoma.* Iridectomy and repeated paracentesis. Enucleation over 3 months from onset.	Mass of organised material in artery from cut end nearly to disc (3 mm.). Contains small vessels. Retinal arteries much thickened. A.C. ∢s blocked. Hge. in ciliary body. (Pictures.)
18. Nuel, Arch. d'Ophth., p. 166, 1896.	F., 53	"Diastolic murmur." Rigid arteries.	Typical picture L. V = hand-movements in part of temporal field; subsequently lost. Some small hges. Cyclitis (Tn.) and enucleation for pain 6 weeks from onset.	Organised mass with blood corpuscles among it at lamina. Organised tissue lifting up and growing under endothelium. Elastica traceable past mass. Artery dilated at situation of obstruction; dilated and empty above it;

				small and blood-filled below. Retinal arteries collapsed and thickened. (Pictures.)
19. SIEGRIST, 27ste Versamml. z. Heideberg, p. 10, 1898.	M., 47	?	Ligature of R. external, and later of R. internal, and common carotids in operating for carcinoma of tongue. On morning after second operation blindness R. Typical picture. Death 6 days later. Obtained *post-mortem*.	Thrombi in carotid, cerebral, and ophthalmic arteries, and in central artery before its entrance into nerve. None more peripherally. (Picture.)
20. MICHEL, Zeitsch. f. Augenh., pt. 2, p. 1, 1899.	M., 58	Widespread arterio-sclerosis. No albuminuria (but *post-mortem* chronic nephritis). Died of hemiplegia.	Typical picture with some hges. in periphery. Some improvement of vision later. Death 5 weeks from onset. Obtained *post-mortem*.	Endarteritis from lamina backwards for 6 mm. Flat and swollen hyaline cells and giant cells. In front of lamina just beyond point of greatest narrowing ($\frac{1}{10}$ of normal) a yellow homogeneous thrombus. Retinal arteries thickened. (Picture.)
21. WELT, Arch. f. Augenh., vol. xli, p. 355, 1900.	F., 34	*Post-mortem* thickened tricuspid. Thrombi in heart. Interstitial nephritis, etc.	Loss of vision after hæmatemesis. R. = fingers at 1 metre; L. = fingers at $1\frac{1}{2}$ metre. Picture of obstruction central artery, albuminuric retinitis and detachment of retina *both*. Detachments disappeared, and V. rose to R. 1/60, L. 1/24. Death 3 weeks from onset.	In R. central artery a thrombus a few days old. In L. central artery no thrombus, but a thrombus in the central *vein*. (Pictures.)

Author.	Sex and age.	Evidence of vascular or renal disease.	Clinical features.	Pathological examination.
22. Galinowsky, Arch. f. Augenh., vol. xliii, p. 183, 1901.	F., 74	Mitral and aortic first sounds impure. Peripheral arteries rigid. No albuminuria.	Blindness of L. 6 to 7 weeks before seen. Disc pale; arteries small. Slight iritis. Later *glaucoma*. Enucleation 2½ months from onset.	For 1 mm. above lamina marked endarteritis completely blocking and distending the vessel. Tapered off at the ends, leaving an eccentric lumen. Contained a calcareous nodule. Round cell infiltration of vein in same situation. (Pictures).
23. Hofmann, Arch. f. Augenh., vol. xliv, p. 339, 1902.	M., 42	Chronic nephritis. Dilated heart.	Sudden blindness L. Typical picture. Later a few hges. R. Death 5 months later. Obtained *post-mortem*.	Organised obstruction 4 mm. long in L. central artery. Not intimately connected with wall. Similar condition in R. with a small blood-filled lumen at one side. (Pictures.)
24. Gonin, Arch. d'Ophth., p. 219, 1903.	F., 52	Mitral insufficiency. Albuminuria. R. hemiplegia 2 years before.	V. of L. lost during erysipelas. Retinal haze; arteries narrow; some striate hges. Vein rather dilated. Flat detachment below macula. Died 3 months later. Obtained *post-mortem*.	Granular mass penetrated by endothelial cells in central artery. Farther forward an organised canalised thrombus in the vein (of older date according to G.).

transversely. In NETTLESHIP'S first case there was undoubtedly an organising plug in the central artery, but whether an embolus or a thrombus it would be difficult to say from the pathological examination alone. The clinical history (aortic disease, sudden blindness without prodromata, etc.) makes an embolus more probable. His second case (NETTLESHIP and WATSON) is more doubtful, as he himself admits. His third case (NETTLESHIP and LAWFORD) seems to be one of endarteritis (? with thrombosis) the result of diabetes, and presents many points of resemblance to Case 2. The obstruction was found in the case of SCHMIDT-RIMPLER, but neither the description nor the picture enables one to come to any certain conclusion as to the nature of the lesion. There is no picture given of PRIESTLEY SMITH'S case, and the description is very brief, so that beyond the fact that the artery was occluded nothing certain can be affirmed. GOWERS states that the masses found by him in the central artery were probably not the original obstruction, since the vessel was collapsed above (proximal to) them. He believes that the true embolus had lodged at the origin of central artery from the ophthalmic, beyond the portion of nerve included in the sections. The association of the obstruction with emboli in the middle cerebral artery and in the kidneys and spleen, make it probable that it was a true embolus however. In POPP'S case nothing was found, and it must be supposed that the obstruction was overlooked (lamina cut longitudinally). It is impossible to believe with Elschnig that an embolus or thrombus can be absorbed and leave no trace. The same remarks apply to HIRSCHBERG'S case. The case of SCHNABEL and SACHS was most likely one of endarteritis—small peripheral lumen clothed with endothelium. No picture is given. MANZ'S case seems to be a typical true embolus closely similar to Schweigger's, Marple's, and Case 1. A very excellent picture will be found in this paper. In ELSCHNIG'S, the pictures clearly show that the lesions described as emboli are endarteritis. There is the typical eccentric endothelium lined lumen and thickening mainly confined to the inner

coat. WAGENMANN'S case is probably of the same nature, but not so certainly so. MARPLE'S is another case of typical embolus analogous to Case 1. In RIDLEY'S paper the picture is far from clear, but from the description it seems sufficiently probable that the lesion found was a thrombus—whether a secondary thrombus or the true cause of the symptoms must be doubtful. The lamina was cut longitudinally. In NUEL'S case the real obstruction seems to have been found. It is an organising mass, presumably a plastic embolus or thrombus. Cardiac disease was present. SIEGRIST'S was undoubtedly a case of thrombosis spreading from the carotid after ligature, but as before stated it belongs to a class different from all the others mentioned. MICHEL'S case is a typical one of endarteritis and thrombosis, much like Case 2 above and Galinowsky's case. WELT'S case is altogether anomalous, both clinically and pathologically. It does not belong to the embolism group, but to the group of cases of blindness following copious hæmorrhage. Leaving out of account the somewhat remarkable fact that detachments of the retina disappeared within a few days in *both* eyes, there remains the explanation of a blindness of some three weeks' duration by a thrombus at most a few days old. Still more remarkable is the statement that while the ophthalmoscopic picture was similar in the two eyes, the central artery was obstructed in one and the vein in the other. The pictures are not more convincing than the descriptions, and the case must be altogether rejected. GALINOWSKY'S case is an excellent example of a nodule of endarteritis in the region of the lamina, and is well illustrated. It bears a very close resemblance to Case 2, except that the obstruction was complete. The pictures given in HOFMANN'S paper show nothing but an artery cut obliquely. The similar condition found in the other eye—in which there were no signs of arterial obstruction—is thus easily explained. It is impossible to accept GONIN'S explanation of his case. He found a granular mass in the artery indeed, but believed it to be a thrombus secondary to a block on the vein. The consequences of

obstruction of the central vein are, however, well known, and bear no resemblance to those of obstruction of the artery. In the same paper GONIN gives a case of severe hæmorrhagic retinitis in which an obstruction was found in the artery. To accept these two cases would be to upset innumerable other authentic records, so that an error of observation must be supposed.

Certain other cases might be quoted from the literature which have a more or less direct bearing on the subject without being in all respects typical. Thus ROTHMUND and EVERSBUSCH state, without giving details, that in a case of "embolism of the central artery" the diagnosis was strengthened at the autopsy by the discovery of a thrombus in the right carotid, middle, cerebral, and ophthalmic arteries. Apparently there was no microscopic examination of the central artery. Again, a case of FRIEDMANN'S lends support to explanations depending upon endarteritis, or endarteritis with thrombosis. A man of 52, without any cardiac or renal lesion, but with rigid radials, became affected with obstruction of the right central artery. A year later he developed spastic paralysis, and $2\frac{1}{2}$ years after this he died of apoplexy. The whole system of basal arteries, down to the smallest twigs, showed obliterative endarteritis, and although the central artery was not microscopically examined, it seems probable that the blindness was due to a similar condition in it probably associated with thrombosis.

The general result of the examination of the literature, therefore, would seem to be that ample proof has been furnished that obstruction of the central artery may be due to one of three causes: (1) embolus, (2) endarteritis alone, (3) endarteritis with thrombosis. Thrombosis without endarteritis probably only occurs in exceptional cases, as where the carotids have been ligatured. There is at present no pathological proof that the obstruction may be caused by hæmorrhage into the nerve or nerve sheath, or by spasm apart from endarteritis.

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The references to cases pathologically examined have already been given in the tabular list. The following is a list of the other papers mentioned in the text; it does not pretend to be a full bibliography of the subject:—

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Wagenmann. Arch. f. Augenh., pt. 2, p. 219, 1897.

Description of Plates III, IV, and V (Figs. 1 and 2).

Plate III.

Fig. 1, × 120.—The central vessels within the lamina cribrosa in Case 1. The lumen of the central artery is occupied by a granular but otherwise structureless mass with a vitreous fracture. It fully distends the lumen, the little cleft at one side being probably artificial. The surrounding connective tissue is dense, but shows no sign of inflammatory reaction, and there has been no attempt at organisation, although the obstruction had occurred three years and two months before. The vein in this situation is in two divisions, both of which are almost or entirely blocked.

Fig. 2, × 120.—The central vessels farther up the nerve in the same case. The artery is to the left, and can be distinguished by the wavy contour in its walls, which represents the elastic membrane of Henle. It is entirely collapsed and obliterated by proliferation and adhesion of its endothelium. The vein is concentrically narrowed by thickening of its walls (not by endothelial proliferation), but a little slit-like lumen still remains lined by a single layer of endothelium. No blood corpuscles were found in it in any of the sections. The nerve is extremely atrophic.

Plate IV.

Fig. 1, × 120.—The central vessels within the lamina cribrosa in Case 2. The central artery is to the left; its lumen is of about the normal diameter, but is almost filled up with a nodule of endarteritis. There is, however, a minute cleft-like lumen in about three-quarters of its circumference, and in this a few red blood corpuscles are visible. The nodule itself consists of blown-out pale cells, similar to those found in the retinal vessels, but with rather better marked cell divisions and more deeply stained nuclei. The dark granular mass in the substance of the nodule is a calcareous patch. For about one-fourth of the circumference the structure is intimately connected with the vessel wall, and over the rest of its surface it has an irregular lining of endothelium. A small branch is given off in this situation, which is completely blocked by endothelial proliferation. The lumen of the vein is encroached upon by fibrous tissue which, in the sections succeeding this higher up the nerve, formed definite trabeculæ dividing the lumen into a number of loculi.

Fig. 2, × 120.—The central vessels higher up the nerve in the same case. The artery is to the left. It is distended, full of blood, and shows no

endarteritis. The distension in this case, as compared with the extreme collapse in Case 1, is probably to be associated with the fact that the obstruction farther down the nerve was not complete. The lumen of the vein is here no longer divided into loculi or encroached upon by fibrous tissue, but it is very small, and there is some cellular infiltration of its walls. Comparison with Fig. 1 shows that the connective tissue surrounding the central vessels is denser at the lamina cribrosa than farther up the nerve (see p. 290).

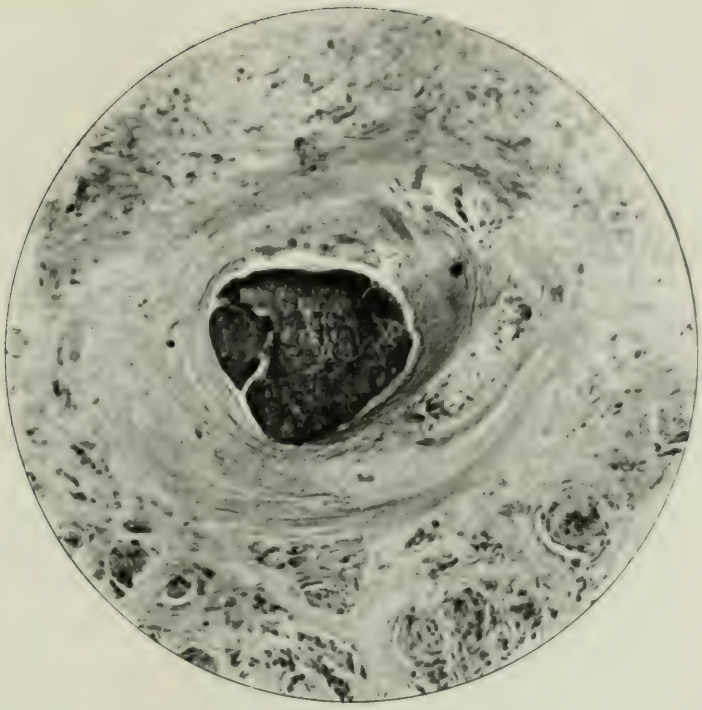
Plate V.

Fig. 1, × 160.—A retinal artery in Case 2. It is a superior main branch, and is probably the one seen ophthalmoscopically to be obstructed. The lumen is quite obliterated by a structure which seems to have been laid down in concentric layers from one side. It shows therefore a faint lamination, and there are a few badly stained nuclei. From the changes found in the other retinal arteries and in the central artery it is probable that the process was one of endothelial proliferation.

Fig. 2, × 160.—Another artery from the same case. This is an inferior branch, and ophthalmoscopically it was not obstructed, and showed only a moderate degree of sclerosis. The process is evidently the same as in Fig. 1, but the obliteration is not complete, a small blood-filled lumen remaining at one side. The eccentric narrowing of the lumen is highly characteristic of endothelial proliferation.

Note.

While these sheets were in the press a long and important paper on vascular disease of the central vessels has appeared, by Harms (Arch. f. Ophth., vol. lxi, part 1, p. 1, and part 2, p. 245). Two cases of obstruction of the central artery are given. In one there was complete obliteration within the lamina cribrosa by an organised thrombus; in the other there was great narrowing of the central artery by endarteritis, with complete obstruction of the superior, and advanced disease of the inferior, retinal arteries. It is impossible here to summarise his results, which in many points agree with mine, and I must therefore be content with referring to the paper.



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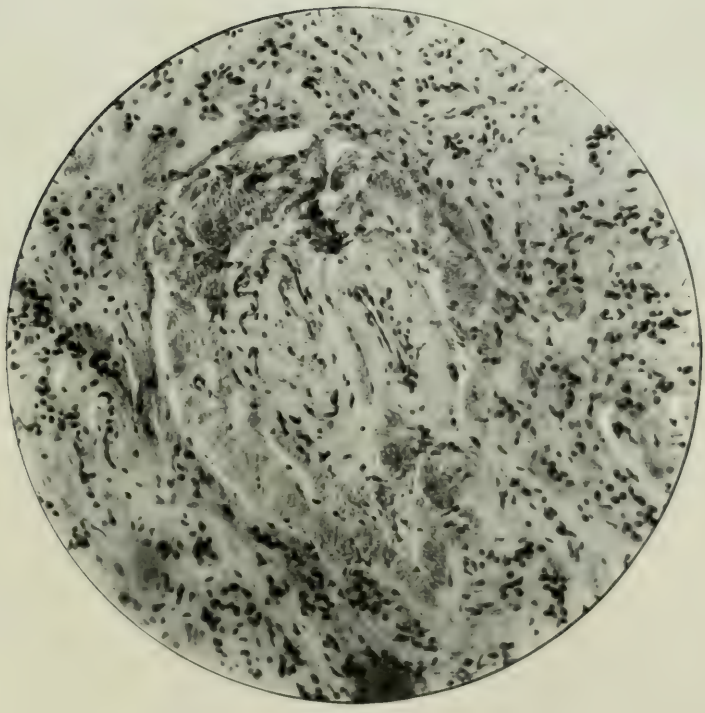

Fig. 2.

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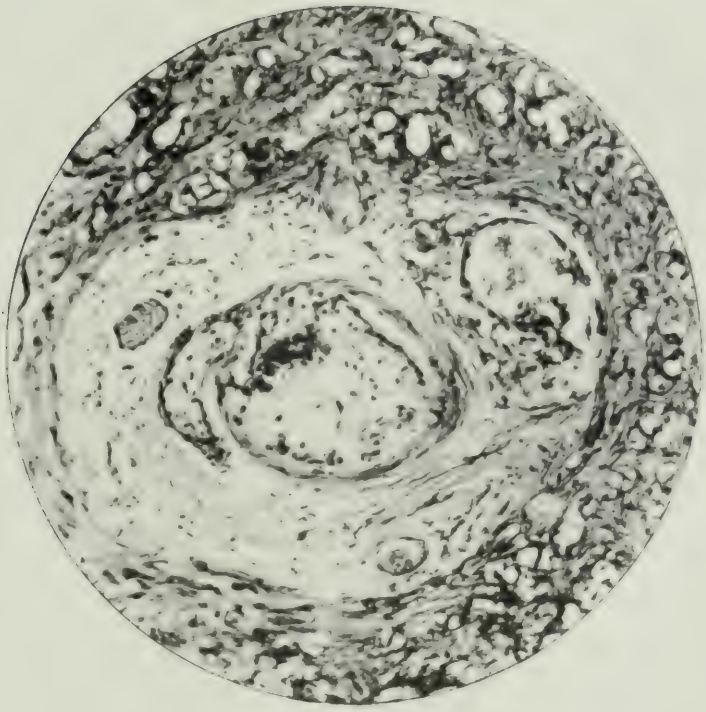

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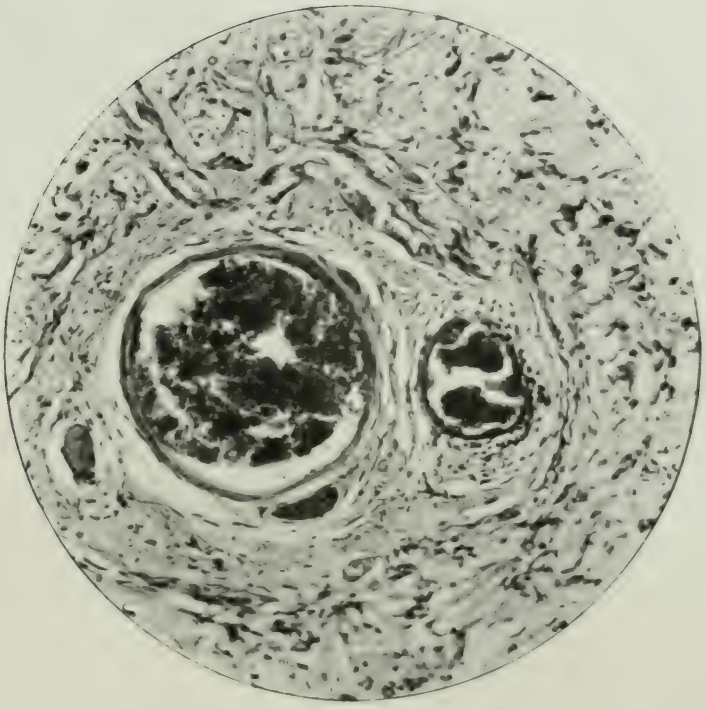

FIG. 2.

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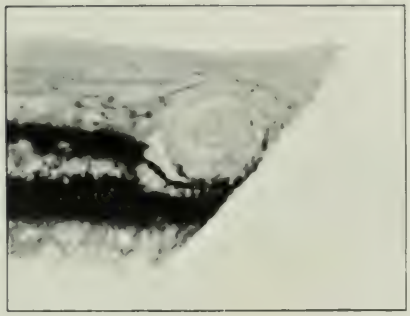

Fig. 1.

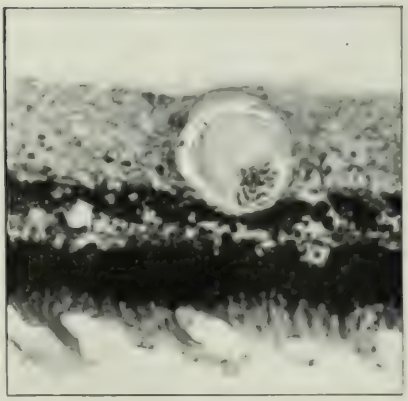

Fig. 2.

Fig. 3.

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MARGINAL BLEPHARITIS: ITS CAUSE, PATHOLOGY, AND TREATMENT.

By Angus Macnab, M.B., F.R.C.S.

The application of bacteriology to the study of the inflammatory affections of the eye has signally failed in some instances to throw light upon the condition present. The same may be said of its application to general medicine. But as in the wider, so here in the more restricted field, its application has elucidated the cause of certain changes, and resulted in great improvement in our methods of treatment by giving us some indicator of progress more definite than mere clinical examination.

When we find a condition variously termed *Ulcerative Blepharitis, Marginal Blepharitis, Sycosis, Chronic Blepharitis, Tinea Tarsi, Tylosis,* without any cause being given for it, or any precedent condition out of which it arises, added to which the existence of many and contradictory methods of treatment, whose only common feature is their uncertainty, we may reasonably conclude that a bacteriological examination to determine the cause of this condition might also succeed in determining its treatment. Such a conclusion has been amply justified.

The bacteriological examination establishes the following facts:—

1. That the majority of cases of marginal blepharitis have the Morax-Axenfeld bacillus in their secretions.

2. This bacillus can be most readily obtained where the lesions are worst, *i.e.*, at the angle and the margins of the lids.

3. During the so-called cured condition, they are very difficult to find, and during relapses they are plentiful.

4. They exist at the onset of the condition, and still flourish after the disease has lasted for a life-time. In short, there is a very definite association of the Morax-Axenfeld bacillus with marginal blepharitis.

It is common knowledge that, amongst the various diseases of the conjunctiva, there is a well-marked type symptomati-

cally classified as "angular conjunctivitis." This has been proved to be due to infection with the Morax-Axenfeld bacillus, the proof even going so far as inoculation on the human subject. The infecting agent, incubation period, course, and treatment of this "angular" conjunctivitis are well known.

Here, then, are two conditions which, bacteriologically, show in common the presence of an organism of proved pathogenic properties in the human eye. The one has a definite onset, determined by inoculation, a course observed clinically, and a termination brought about by treatment. Untreated, it seems to lose its clinical entity, and pass into that chaos commonly known as chronic conjunctivitis. The other evolves itself out of the chaos, is vaguely recognised as a type, is profusely named, and occasionally cured. Its cause is not known; it is vaguely supposed to follow on a conjunctivitis; because it must follow something, and that is the most likely.

The relation between these two conditions is that they are stages of one and the same disease—"chronic blepharo-conjunctivitis." Every possible intermediate gradation between the extremes can be found, and when tested with the indicator which the microscope gives us, will show the proof of their identity, *i.e.*, the presence of the Morax-Axenfeld bacillus. They should therefore no longer be described separately, and classified as two distinct diseases.

This disease, "blepharo-conjunctivitis," has a very definite clinical history; its pathology and bacteriology can be determined, certain complications may occur during its course, and it responds rapidly to proper treatment.

The early stages are well known, and only a short *résumé* of the main facts regarding them will be given here.

The infection is probably through close contact, as in the cases of family and school epidemics, or through infected dust blowing into the eye, the organism having great resistance to dryness. After a latent period of about 36 hours there is an itchiness at the lid margins, with a dry or gritty sensation in the conjunctiva. In the morning the lids are heavy and stick

together. A glutinous white secretion collects at the outer and inner angles of the palpebral fissure, especially at the inner, and on the caruncle, which is red and slightly swollen. Several days later the margins of the lids redden. The normal smooth, shining, clean surface between the outer and inner lid borders changes progressively from the angles towards the centre. It becomes dull, sticky, moist, and deep red in colour. Along the roots of the cilia a whitish, glutinous secretion collects, and gums them together into tufts. The skin of the lids immediately outside the angles is red and moist; further out it is coated with the dried secretions. The cornea is not affected. The bulbar conjunctiva usually shows a light injection, not, however, affecting the circumcorneal region. At this stage each eye presents the appearance of being surrounded by two intensely-red V's lying on their sides with their apices directed away from each other; this is produced by the contrast of the red intermarginal lid border against the white sclerotic. The caruncle is now intensely injected and covered with secretion. When the lids are everted the conjunctiva is seen to be very little affected; there is often a slight velvety thickening on the lower lid, but this is always less marked at the fornix than near the lid border.

Usually a day or two after the onset in one eye, the other is attacked in an exactly similar way; and subsequent stages in the disease are therefore bilateral.

After three or four weeks the diffuse, intense redness of the intermarginal surface changes; the epithelium has been macerated and cast off; dull red blotches, at first very small, but afterwards increasing in size, appear near the roots of the cilia; these form definite excoriations, from which comes a serous exudation. Crusts form on the cilia and at their roots. If these are removed the red excoriations show beneath. Sometimes the conjunctival discharge is very free, and bordering on the lid margins is a skin region, moist, macerated, excoriated, intensely injected, and covered with a thin, whitish secretion. The subjective phenomena, burning,

itching, and pain, are well marked, and sometimes there is considerable photophobia. The part taken by the conjunctiva of the lids is much greater. It is quite thick and velvety, being even thrown into folds. The bulbar portion is injected, and sometimes even a little chemotic. These acute conditions are rare, and may be due to mixed infections.

Let this condition persist for years, and in a considerable number of the cases an ulcerative marginal blepharitis will develop, which is extremely chronic in type, and under the usual treatment of yellow oxide, massage, etc., may last for years—in fact, often recurring at intervals for the rest of the patient's life.

The changes are almost entirely confined to the free border of the lids and the skin adjoining. In health the free border of the lid presents an inner, or posterior, rectangular, sharp margin, which is adapted accurately to the globe, and, when the eye is shut, to its fellow opposite. The corresponding outer or anterior margin is also sharply cut, and forms an angle slightly acute, along which project the cilia. Between these two margins lies the smooth, flat, shining intermarginal portion, marked by a line of round lighter coloured spots—the mouths of the ducts of the Meibomian glands—parallel to the root sheaths, and rather nearer the posterior edge. The adjoining skin is loose, very soft and pliable, and slightly redundant.

The inner lid margin adheres to the globe by surface tension, the intermarginal portion being continuously oiled, remains dry, and there is no tendency to epiphira.

Contrasted with this, in marginal blepharitis we have the presence of ulceration, the destruction of this beautifully-moulded lid margin, the loss of many cilia, and changes in the adjoining skin and conjunctiva.

The process of excoriation of the epithelium progresses after the underlying corium is exposed until the inner and outer lid margins, along with the intermarginal area, have been destroyed by ulceration. Temporary healing takes place at parts, where we see an irregular rounded border, not

accurately adapted to the globe, showing a few scattered Meibomian duct orifices and irregularly-placed hair follicles.

At other parts are thick crusts, through which tufts of cilia protrude, and scabs which cover up the destruction which is going on. Some of the hair follicles become infected with pus forming organisms (Staphylococcus usually), so that we see occasionally a small abscess from which a hair projects. Where temporary healing has occurred, the newly-formed skin again becomes macerated and the process repeats itself anew. Throughout there is a definite tendency for the canthi to be more affected than the mesial portion. Occasionally the canaliculi become closed, but this is uncommon.

This continual contraction of the scars along the margin of the lids causes a degree of blepharo-phimosis, which mostly affects the outer angle. The skin, especially of the lower lid, being drawn upon and continuously absorbed in the ulcerative process, loses its pliancy, is shortened and thickened, producing an ectropion usually of very slight degree, and a difficulty in closing the lids. The upper lid is thickened near its margin, so that it has a heavy rolled-up appearance, the skin is smooth, dense, and reddened, around the canthi we can always see the moist, macerated area on which the gummy whitish secretion collects, which was so typical of the early stages.

In cases where the ulceration is rapid, the conjunctiva is everted, turning out to the lid margin, and forming a deep red, smooth, shining line between the white sclera and the crusts, which mark the true lid border.

In the extremely slow and chronic cases, which may have lasted without very much destruction for 20 or 30 years, it is more common to find some entropion and trichiasis, especially of the upper lid.

A marked feature is the deficient power of closing the lids; this should be completely done without contraction of the frontal portion of the orbicularis palpebrarum, but in some of these patients when they are told to gently close their eyes, about 2 to 3 mm. of sclerotic remain

visible below the upturned cornea. This is only covered by contraction of the whole orbicularis, when the skin is wrinkled by the strain put upon it.

Many of these patients have their canaliculi slit up and their nasal ducts probed; this being repeatedly done adds a nasal duct stricture to their blepharitis, and changes the case from a simple one amenable to treatment to an extremely intractable form of lachrymal stenosis.

Although ulcerative marginal blepharitis is quite common, yet considering the enormous frequency of diplobacillary conjunctivitis, it is obvious that only a limited proportion of the cases reach this stage. The angular conjunctivitis stage remains often for many years. In some cases the lid condition is very slight, but the patients seem to develop very readily ulceration of the cornea. These ulcers are usually called "catarrhal"; they are shallow, oval, or round, with faintly infiltrated base, and readily heal, leaving a small facet. Occasionally a little hypopyon is found, and rarely does the ulcer penetrate deeply with a tendency to perforation. Unsuitably treated, these are very chronic, patients have informed me that they have had "scores of ulcers"; but if the condition be correctly diagnosed, and the treatment directed to the conjunctiva, a good result can easily be obtained.

Pathological Changes.—The chief changes take place in the epithelial layers of the lid margins, but there are also some in the deeper parts, the tarsal plate itself being affected. The epithelial changes occur mostly at the lid margin; here in the intermarginal portion there is an increase in the squamous, keratinized elements of this transitional epithelium, making it more resemble skin. The deeper layers of cells have proliferated, and sent processes down into the corium, so that the epithelial coat varies very greatly in thickness; at some places, that is, opposite these processes, it is very thick; at others, between them, it is reduced to one or two cells in thickness, and where thus reduced we find the subjacent corium densely infiltrated by small cells. These places correspond to the macerated red patches observed clinically. The

thinning may go on to such an extent that the corium is actually exposed, and then we have an ulcer formed, which increases in size by confluence of such exposed spots. Such ulcers, however, remain quite shallow, and their bases contain the processes of epithelium as small islets of cells which have a continuous tendency to spread out and re-cover the denuded surface.

In the granulation tissue formed by vascularization of the small-celled infiltrate there is a continuous contraction going on, dragging on the internal or posterior lid border, thus narrowing the lid margin, and causing slight ectropion of the conjunctiva.

Where such ulcers have healed the lid is covered by several layers of a stratified squamous epithelium, under which is a non-vascular cicatricial fibrous tissue.

The root-sheaths of the cilia are atrophied, and surrounded by a small-celled infiltration; they are very much reduced in numbers, and some are altered in direction.

The Meibomian glands are dilated, some cystic, their ducts are often obliterated by the ulcerative process, those remaining open irregularly.

The inner lid margin cannot usually be defined; at the limit of the conjunctiva there is a thickening of the epithelium to form many layers of cells, here the surface falls away from the bulb, and the area of ulceration begins. This rounded irregular line corresponds to the situation of the inner lid border.

In the conjunctiva there is a marked increase in the number of goblet cells, and the epithelium rests upon a densely infiltrated layer of the corium, especially towards the lid margin; these changes diminish as we pass to the formix, where the conjunctiva is almost normal.

The bulbar conjunctiva is normal; in fact, any change which may exist here is related to some coexisting or previous conjunctivitis.

The tarsal plate shows changes throughout in the lower lid, and at its lower margin in the upper; there is an infil-

tration with small round cells, and fibrous tissue formation, causing thickening and distortion, usually a slight entropion of the upper plate, and ectropion of the lower.

The lids, both upper and lower, are distinctly shorter than normal.

Bacteriology of the Condition.—The only constant, and in the writer's experience almost invariable organism found in these cases is the diplobacillus of Morax and Axenfeld. It is found in the gummy secretion collecting about the angles, in the crusts at the roots of the hairs, and in the moistened scabs which cover the ulcers. In the old confirmed cases it naturally can rarely be obtained in pure culture. But its constant presence, and the gradual evolution clinically of the ulcerative stage of the disease, from a slight "angular conjunctivitis," which is certainly due to a pure infection with this organism, make its causal connection with the disease absolutely certain.

The organism itself when in young culture, or from a recent case of blepharo-conjunctivitis, has the following morphological characters. The bacillary form is constant. The rods are from 1·5 μ to 3 μ in length, and 0·5 μ to 1 μ in breadth. They are quite straight and even in calibre, the ends being slightly rounded. They lie end to end in pairs, these pairs may form chains; single rods are also occasionally seen.

The protoplasm shows a tendency to stain more deeply at the ends of the rods than in the middle. Capsules are readily seen by special staining, and sometimes even in a methylene blue preparation. The bacillus is gram-negative, and can only be confused with that variation, which has been given a special name, *B. liquefaciens*, by Petit.

The form is very constant in smear preparations from recent cases, or in young cultures. From old blepharitis cases, while some of the organisms are of this typical shape, others vary from it so much as to be almost unrecognisable. Large single round or oval bodies, more refractile than the small ones, are not uncommon. Double cocci, kidney shaped, with their concavities together, and of 2—3 μ in diameter, are

more common. Tetrad groups, and perfectly round bodies in short chains of paired individuals, also occur. These are all of large size and gram-negative, although not so easily decolourised as is the small rod form.

That these grotesque shapes are really vagaries of the diplobacillus is certain, as all grades in shape between them can be found; and if a culture be taken from a case of long standing blepharo-conjunctivitis, the pure colonies isolated, and reproduced on fresh medium, the transition is very clearly seen. After about 4 or 6 hours' growth, from the large oval bacillus a short chain is formed, the centre of which is formed by two oval bodies, several times the thickness and length of the ordinary organism; at each end of the chain is a pair of typical diplobacilli, and the different intermediate stages are seen between. Where a large round "spore" has broken up we find very regular rosettes, the centre formed of two or three round bodies from which radiate out lines terminating in typical diplo-forms. In these colonies the parent has broken up at first by irregular cleavage planes, but later by transverse division. The same culture in 24 hours will have lost most of the irregular forms; and in 48 the smears show typical diplobacilli with occasional oval hefa-like bodies distributed through them.

To obtain a specimen showing the typical form without any of these variations, it is best to grow the bacillus on agar with ascitic fluid added; the growth is rapid, and if second and third sub-cultures are made each 24 hours old, the type will be found practically constant.

From the conjunctiva direct, the typical form is obtained in great numbers from cases of early angular conjunctivitis of about a week's duration, especially when it is the first attack, and where there is much secretion. The large forms are readily obtained in old standing blepharitis, and in recurrent attacks of angular conjunctivitis in the early stage. In fact, their presence indicates the chronicity of the case; the writer has found that it is quite feasible to give an opinion from the appearance of the secretion-preparation, as

to whether the case is an old one or a recent infection, and thus control patients' statements as to the duration of the disease, and the existence of previous attacks.

The diplobacillus grows on a limited range of media. On Löffler's blood serum and ascites agar it can be grown with certainty. In pepton broth a very slight growth, and on the other commonly used media not containing blood or human serous fluids no growth is obtained. That variety described by Petit, and further examined by the present writer, shows, in general, a more vigorous growth, and also the additional power of growing on pure agar, in other respects it has no essential difference.

Ascites Agar Growth.—Single colonies grow superficially, in a stroke culture, as transparent drops, which afterwards become grey and more opaque. These coalesce and form a greyish slime, which looks brownish in transmitted light. In from 3—8 days at 37° C. the growth reaches the sides of the tube, and later a brown discoloration spreads into the medium.

On blood serum (Löffler) at 36° C. In 12 hours, when the culture is made from a fresh case, single colonies are seen in the form of clear, transparent moist spots, slightly excavating the surface. These begin to coalesce in about 24 hours, and the liquified medium runs down to the bottom of the tube, leaving hollows and furrows on the surface, which when examined by transmitted light show brownish coloured bases. The medium takes on a brown discoloration, which deepens with age. The ordinary type of diplobacillus often dies out when repeatedly transferred from one serum tube to another, the Petit type is more resistant and can be cultivated on this medium for an indefinite time.

The resistence of the organism against heat is very low, after 5 minutes on a water bath at 55° C. the culture is killed. Dryness, on the contrary, has very little effect on the organism, after 14 days' drying at 37° C. they retain their vitality.

Treatment.—The researches of Morax and Axenfeld have shown the great value of the use of sulphate of zinc in the

treatment of angular conjunctivitis. A collyrium of 2 grs. per ʒi is dropped into the conjunctival sac three times a day until the organisms disappear from the secretion, when the strength can be reduced to 1 gr. per ʒi.

The greatest benefit is obtained in the late stages of the disease, when there is ulcerative blepharitis, by the same treatment. A preliminary cleaning of the lids from crusts and scabs, by the use of a warm bicarbonate of soda lotion and careful wiping along the edges, allows the zinc better access to the organisms. An ointment of oxide of zinc 20 grs. per ʒi should be ordered to be applied along the lid margins at night. With this treatment the ulceration of the lids rapidly disappears, and the organisms are no longer found in the secretions. The strength of the zinc drops can now be reduced to 1 gr. per ʒi, which is, of course, much less irritating. If there is much associated thickening of the conjunctiva, an occasional painting with silver nitrate, 10 grs. per ʒi, and careful neutralisation with saline, is very useful.

When the active changes have ceased, massage with a diluted yellow oxide of mercury ointment, 4 grs. per ʒi, will assist in diminishing the thickening of the lid margins.

Ectropion of the punctum, blepharo-phimosis, entropion, and trichiasis may need surgical treatment on the ordinary lines for such affections.

The tendency to recurrence is very great. Treatment must be kept up for at least one month after all active changes have disappeared.

Conclusion.

A large proportion of the cases, clinically termed ulcerative marginal blepharitis, belong really to the disease called blepharo-conjunctivitis or diplobacillary conjunctivitis. They can be fairly accurately distinguished clinically; and microscopically with certainty. Their cause is an infection with the Morax-Axenfeld diplobacillus. The disease is not self-limited, and spontaneous cure is rare.

The treatment by the use of sulphate of zinc gives the best results.

ON IMPLANTATION DERMOIDS OF THE CONJUNCTIVA.

By M. S. Mayou.

So little has been written on the subject of Implantation Dermoids of the Conjunctiva that Cirincione[1] goes so far as to doubt that they occur. So far as the literature of the subject goes there are cases on record by Uhthoff[2] and E. T. Collins.[3]

Implantation Dermoids of the Conjunctiva arise in two distinct ways :—

(*a*) By the down growth of the surface epithelium of the conjunctiva following a wound of that membrane, the connection with the surface epithelium becoming subsequently cut off by atrophy, due to pressure of the newly formed fibrous tissue. That this method of formation no doubt occurs not infrequently, I have shown elsewhere.[4]

(*b*) Direct carrying in of the conjunctival epithelium by a foreign body. That this method of formation does occur has not been previously proved, as in the two cases mentioned above the cysts were not cut in serial section, so that positive evidence that there was no connection with the surface epithelium was wanting, and the length of time existing between the injury and the examination of the specimens may have caused its disappearance if present. I had the opportunity of examining a case one week after the bulbar conjunctiva was injured by a chip of wood striking it.

F. M., male, æt. 11.—On November 2nd, 1902, five days before being seen, the patient was breaking a piece of wood, and a piece flew up and struck him in the right eye. It pained him at the time, but he did not take much notice of it until two days later a "blister," as his mother described it, appeared on the outer part of the right eye.

On admission there was a red swelling, having the appearance of a large phlyctenule, on the outer part of the bulbar conjunctiva in the palpebral aperture, about 6 mm. from the limbus. There was no photophobia and the conjunctival injection was more or less limited to the area surrounding the swelling. No foreign body could be seen. As its nature was doubtful, it was excised. It was not adherent to the underlying sclera. A stitch was put in and the wound healed by first intention.

The specimen was hardened in alcohol and serial sections made, stained with logwood and eosin and by Pappenheim's method. The wound on the surface had not become completely covered with epithelium, but beneath the gap in the epithelium there was new fibrous tissue. The position of the cyst with regard to the entrance wound was somewhat oblique, the piece of wood having evidently passed obliquely beneath the surface epithelium. Inside, the cyst contained the splinter of wood causing the injury, as well as many mononuclear and polynuclear cells of all types, a few degenerated plasma cells, and one or two giant cells. The epithelium lining the cyst was for the most part three or four cells in thickness, of the type found on the surface of the bulbar conjunctiva; it surrounded the wood with the exception of a small area opposite to the entrance wound, the epithelium having evidently been carried in in front of the splinter, and then grown round it, as there was evidence of recent mitosis having occurred in the cells at the ununited ends. No process of epithelium could be found in any of the sections connecting the surface epithelium with that of the cyst. Around the cyst there were numerous new and dilated vessels which showed enormous proliferation of their endothelium, with very active diapedesis taking place. The tissue also around the cyst contained numerous leucocytes, plasma cells, and giant cells. The exudation was situated around the vessels, many of these vessels having both endothelial and perithelial coats and some intermediate tissue; in fact, their walls were of such thickness that it is impossible to believe that cells having so little amæboid movement as lymphocytes and plasma cells can have made their way through them.

Another curious point was that some polymorphonuclear and

even some of the mononuclear cells were stained a brown colour. These cells were lying side by side with normally staining cells. They were found in greatest numbers near the chip of wood, to which their brown colour was evidently due, but they were also found in the vessels in the neighbourhood of the wound. If this was due to the ingestion of some material (? tannin) from the wood *ante-mortem*, some of the polynuclear cells must have made their way back into the vessels, which is against the generally accepted view. But much stress cannot be laid on this as it is possible that it may have been produced *post-mortem*, although the general appearance did not suggest it, since these brown cells lay side by side with normal staining cells.

Conclusions.—The fact that there was no process of epithelium connecting the surface epithelium with the epithelial cyst wall, and that the cyst wall was even deficient towards the surface wound in an implantation cyst of such an early date as this, disproves the theory that all these implantation dermoids are due to down growth of epithelium from the surface, and although the other form of implantation dermoid does undoubtedly occur, carrying in of the epithelium also takes place.

Case 2.—The mode of formation in this case is much more indefinite than in the case previously described, but shows well the subsequent changes in the epithelium.

C. S., male, æt. 40.—Seen September 4th, 1903. Came to the hospital complaining of a small swelling on the outer side of the bulbar conjunctiva of the left eye. Strong, healthy man. Had at different times received injuries from foreign bodies striking the eye.

On the outer side of the left eye was a semi-transparent swelling about the size of a large pea, evidently containing fluid, with no injection around. He had noticed the swelling two months before, and it had gradually increased in size. The cyst was removed entire, and the wound closed by stitches. Primary union followed.

The specimen was hardened in alcohol, embedded in paraffin and cut in series. The epithelium of the bulbar conjunctiva

covering the cyst was similar to the surrounding epithelium, except that the cells on the surface were more flattened. Between the cyst wall and the surface epithelium was a layer of connective tissue containing blood vessels, a few lymphocytes, and a considerable number of mast cells. No process of epithelium was found connecting the epithelium of the cyst with the epithelium of the bulbar conjunctiva. The cyst itself consisted of an outer wall of slightly thickened connective tissue and was lined by epithelium throughout its whole extent. It varied considerably in thickness from four or five cells up to ten or twelve.

The cells were not flattened but rather of a columnar shape. Tuft-like processes were present in which the columnar shape of the cells was still more marked. Scattered amongst these columnar cells were round and oval cells which were most apparent towards the free margin of the tufts. These cells were clear and non staining, and were evidently epithelial cells undergoing mucoid changes, probably supplying the interior of the cyst with the fluid with which it was filled.

References.

(1.) Cirincione. Deutschmann's Beiträge zur Augenheilkunde, part lv, 1903.
(2.) Uhthoff. Berlin. klin. Woch., 1879.
(3.) E. T. Collins. Researches, 1896.
(4.) Mayou. Hunterian Lectures, 1905.

Description of Fig. 1 and Plate VI.

Fig. 1.—Section through the entire implantation dermoid (Case 1):—

A. Epithelium.
B. Wound through which the piece of wool entered.
C. The epithelium lining the cyst.
D. Piece of wound surrounded by leucocytes.
E. Newly formed vessel in the neighbourhood of the cyst.

Plate VI.

Fig. 2.—Epithelium (Point C, Fig. 1) lining the cyst cavity; many of the cells have two nuclei, and there is evidence of recent mitosis having occurred in some of the cells:—

F. Giant cell in the neighbourhood of the cyst wall.
G. Epithelial cells on the inner side of the cyst wall.

Fig. 3.—A portion of the wood in the interior of the cyst :—

H. Wood.

I. Giant cell.

I′. Polymorphonuclear leucocytes, the staining reaction of some of which is altered by the presence of the wood, I″.

J. Mononuclear leucocytes, do. do. do.

Fig. 4.—A vessel (marked E, Fig. 1) :—

K. Endothelial lining to vessel.

L. Polymorphonuclear leucocytes, some of which are altered in their staining reaction similarly to those found around the wood, L′.

M. Mitosis in a perithelial cell.

$\frac{1}{12}$-in. obj., No. 8 eye-piece.

Fig. 5.—Cyst of the ocular conjunctiva (Case 2) :—

A. Surface epithelium.

B. Connective tissue wall.

C. Epithelial lining which has proliferated into tuft-like processes.

D. Cells undergoing mucoid changes (stains—logwood and Van Gieson).

$\frac{1}{12}$-in. oil immersion, No. 4 eye-piece.

Fig. 1.

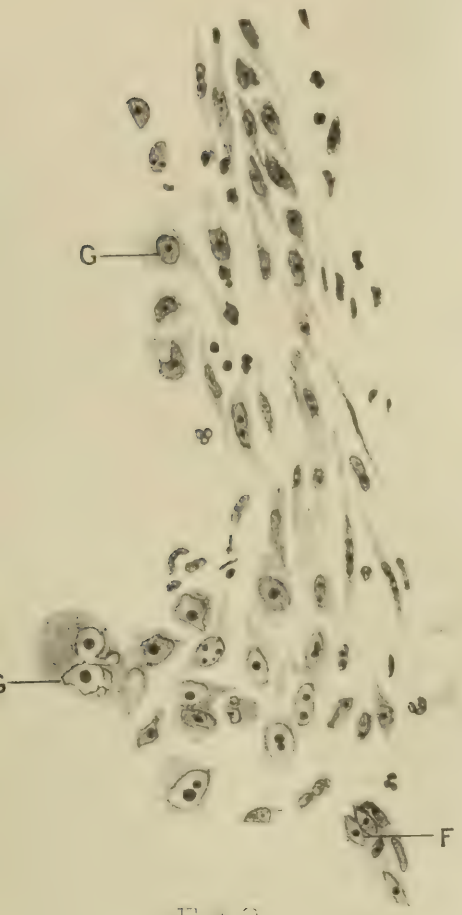
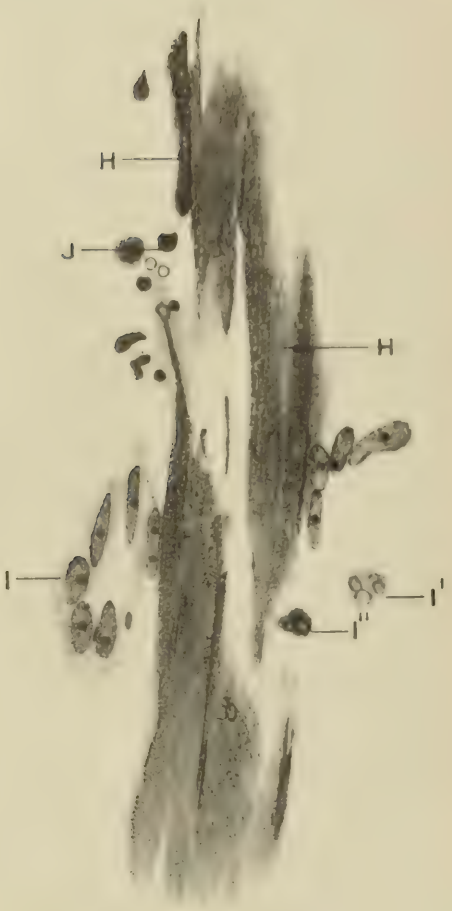


Fig 2.



Fig

Fig.4

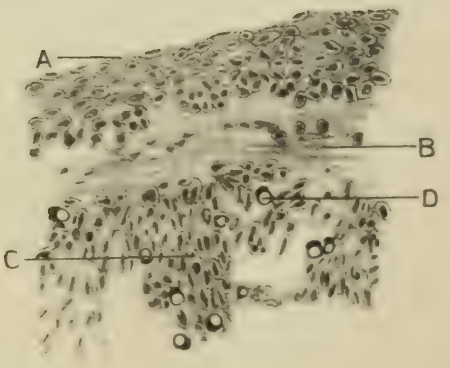


Fig. 3

GLIOMA RETINÆ.*

By S. A. Owen.

Since the appearance of the last article upon this subject by Mr. Marshall (in the Ophthalmic Hospital Reports, vol. xiv), 24 cases of glioma retinæ have occurred in the practice of the hospital. These 24 cases represent 26 eyes. In addition to these a record is given of 26 cases (= 28 eyes) obtained from private sources:—

Mr. Bullar	1 case	No. 425 O.P.
„ Fisher	1 „	„ 644 O.P.
„ Lang	2 cases	„ 244 O.P.; 494 O.P.
„ Lawford	2 „	„ 482 O.P.; 595 O.P.
„ Lawson	1 case	„ 477 O.P.
„ Maddox	1 „	„ 542 O.P.
„ Marshall	1 „	„ 652 O.P.
„ Milligan	1 „	„ 420 O.P.
„ Morton	2 cases	„ 328 O.P.; 412 O.P.
„ Nettleship ...	1 case	„ 397 O.P.
„ Parsons	1 „	„ 657 O.P.
„ Ridley.....	3 cases	„ 211 O.P.; 288 O.P.; 342 O.P.
„ Rockliffe	5 „	„ 222 O.P.; 456 O.P.; H.R.I. (*a*); H.R.I. (*b*); 654 O.P.
„ Sinclair	1 case	„ 541 O.P.
„ Spicer	1 „	„ 358 O.P.
„ Tweedy	1 „	„ 335 O.P.
„ Worth	1 „	„ 650 O.P.

My best thanks are due to these gentlemen for allowing me to make use of their cases. In all instances, except where it is definitely stated to the contrary, the clinical diagnosis has been confirmed by the microscope. Cases presenting any doubtful features have been discarded.

* Read as a thesis for the M.B. degree before the University of Cambridge, July, 1905.

The object of the present paper is to bring up to date the subject of glioma in the Reports. It is based on lines precisely similar for the most part to the two preceding papers on the same subject. (*Vide* Ophthalmic Hospital Reports, vol. xiii; Notes on Glioma, with a Report of 60 Cases by Messrs. Lawford and Treacher Collins; also Reports, vol. xiv, Notes on Glioma Retinæ, by Mr. C. D. Marshall.)

The present paper differs from its predecessors in that a brief abstract is given, as far as possible in each case, of the curator's report, from the macroscopic as well as from the microscopic point of view. Inasmuch as it represents in a condensed form the more important details, it may prove of value to those who are unable to gain access to the museum reports, and who wish to compare the features of these cases with specimens elsewhere.

The conclusions to be drawn from the present series are practically identical with those stated in the two former papers already mentioned. The 60 cases reported by Messrs. Lawford and Collins occurred within the years 1871–1890. Five of these were obtained from private sources. The 32 cases reported by Mr. Marshall occurred between the years 1890–1896. Four were private cases. The 50 cases, which make up the present series occurred between 1896–1904. Twenty-four were patients at Moorfields. The remainder are obtained from private sources. Thus, during a period of 33 years, there have been 107 cases of glioma treated at this hospital:—

1871—1890	55 cases in	19	years.
1890—1896	28 „	6	„
1896—1904	24 „	8	„
Total... 33 years	107 cases.		

The annual incidence in the present series is as follows:—

1896—1897	.....	2 cases.
1897—1898	.....	3 „
1898—1899	.....	4 „
1899—1900	.....	3 „
1900—1901	.....	0 „
1901—1902	.....	2 „
1902—1903	.....	8 „
1903—1904	.....	2 „
Total... 8 years		24 „

Sex.—Of the 50 cases now under consideration, 15 are males and 24 females. The sex in 11 cases is not stated. These figures show a decided preponderance of females. In the earlier papers, in one case males predominated, in the other the sexes were almost equally divided.

The following table shows the relative proportion of the sexes when a large number of cases are considered :—

Authority.	Males.	Females.	Not stated.	No. of cases.
Hirschberg	37	24	16	77
Vetsch	11	11	—	22
Lukowicz	11	15	1	27
Knapp	6	1	—	7
Lawford and Collins	30	27	3	60
Marshall	15	17	—	32
Wintersteiner	221	208	—	429
Present series	15	24	11	50
Total	346	327	31	704

The Eye Affected.—In the present series both eyes appear to have been involved in four cases only (viz., 5,610, 6,676, 425, O.P., 652, O.P.) The right eye alone was affected in 17 cases, and the left eye alone in 14 cases. In 15, the side involved is not mentioned. In view of the last statement, it would be unwise to draw any conclusions in regard to the proportion existing between bilateral and total cases. The usual figure given is one fourth. The figures appended below appear to bear out this statement for the most part :—

Authority.	Bilateral.	Unilateral.	Total cases.	Proportion of bilateral to total.
Lawford and Collins ...	12	43	55	1 : 4·58
Marshall	12	20	32	1 : 2·6
Wintersteiner	97	308	405	1 : 4·17
Hirschberg	14	46	60	1 : 4·2
Vetsch	1	21	22	1 : 22

Of the four cases where the disease was bilateral, in No. 5,610 the left eye had been shrinking since the child was 5 months old. A white spot had been noted in the R. when the child was was only 3 months old. Advice was not sought until the child was 2 years old. The left eye was then excised. Seven months later the child was rapidly wasting. The subsequent history is unknown.

In No. 6,676 we again have to deal with a shrunken globe (the right). The child had been blind in the right eye apparently since 8 months old. The right eye was removed at the age of 1½ years. The patient died about 6 months after the original operation.

In another case (O.P. 425) the left eye commenced to give trouble in May, 1900. It was enucleated in February, 1901. The right eye was noticed to be abnormal in January, 1900, the left media at that date being clear. In this case, then, although apparently the disease was first noted in the right eye, it made more rapid progress in the left. At the time the left eye was enucleated a mass of growth was left behind at the back of the orbit. This could not be removed.

No details of the course of Case 652, O.P., are given. Of the four bilateral cases just related, in one only (652, O.P.) were both eyes removed simultaneously.

Age at which the Growth became Apparent.—It would appear to be quite impossible to draw any accurate conclusions from a study of the dates, which are given in the fourth column of these tables. In many cases no mention is made, in others equivocal statements occur, *e.g.*, "Blind since 2 years"

(No. 5,585). Omitting then such cases, there are 21 cases (= 23 eyes) in which an approximate statement is made of the age at which the growth was first noted by the parents.

In the present series in no instance was an abnormal appearance noted actually at the time of birth.

In one instance only was the growth detected *before the first month*. In this case (Mr. Nettleship's case, 397, O.P.) the father was a medical man. He noticed a white reflex and vessels 3 or 4 weeks after birth. When 7½ weeks old the eye became rapidly inflamed and swollen. This subsided, however, in a few days. The eye, when removed, was small and shrunken. The optic nerve was apparently not involved. After history unknown.

In 3 cases attention was drawn to the eye between the first and second months of life (viz., Cases 5,299, 5,404, 335, O.P., at 6 weeks, 2 months, and 2 months respectively). The subsequent history of Case 5,299 could not be ascertained. The child was operated on when 12 weeks old.

Case 5,404 was operated on when 1½ years of age and was reported alive and well in February, 1905.

Case 335, O.P., was operated on when 3 months old; the growth having been noted 1 month previously. Exenteration was performed 6 weeks afterwards.

Between the second and fourth months, 2 cases (viz., 5,610, right eye; 425, O.P., right eye; at 3 months and 4 months respectively).

In both cases the two eyes were involved. Both patients are in all probability dead. In Case 5,610 this eye (the right) was not involved to the same extent as the left, although it was the eye to which attention was first drawn. For the history of the left eye see p. 328.

In Case 425, O.P., the right eye again was the first to attract attention. The left, however, was enucleated when the child was 1½ years old.

Three cases occurred between the fourth and sixth months of life; viz., 5,610, left; 425, O.P., left; 5,935; at 5 months, 6 months, and 6 months respectively.

The left eye of Case 5,610 was enucleated when the child was 2 years old. It was a shrunken globe. The left eye of Case 425, O.P., was removed when the child was $1\frac{1}{2}$ years old.

Case 5,935 was not operated upon till 2 years old and died within 7 months.

One case between 6 months and 1 year, viz., 5,639, at 8 months. This patient was operated upon when 11 months old. Unfortunately her subsequent history is unknown. The optic nerve was involved near the ocular end and showed much cell proliferation.

One patient at 12 months (viz., 288, O.P.). The eye was removed when $1\frac{8}{12}$ years old. Died 9 months after.

Between 1 year and $1\frac{1}{2}$ years, 2 cases (viz., Nos. 5,123 and 5,383, at 1 year and 3 months, and 1 year and 2 months). The former patient had her left eye enucleated when 2 years old. She is alive and in good health 7 years and 11 months after her operation. The latter patient was operated on when 3 years and 2 months old. No reply was obtained to enquiries in January, 1905. The optic nerve was apparently quite unaffected.

There are 2 cases occurring between $1\frac{1}{2}$ and 2 years (viz., Nos. 6,636 and 6,658: at 2 years and at 1 year 9 months respectively).

The former case was 3 years old when the right eye was removed. She died 2 months after the operation. The latter case was operated on 4 days after attention was first drawn to the condition, his age at that date being 1 year and 9 months. His subsequent history cannot be obtained.

Between 2 and $2\frac{1}{2}$ years, 1 case, No. 211, O.P., at $2\frac{1}{2}$ years exactly. The patient will be referred to subsequently. He is probably alive and well at the present. He was aged 3 at the time of operation.

Between $2\frac{1}{2}$ and 3 years attention was first attracted in 4 cases: viz., 5,545, 6,799, 6,834, H.R.I. (*a*), at $2\frac{10}{12}$ years, at $2\frac{11}{12}$ years, at $2\frac{9}{12}$ years, and $2\frac{7}{12}$ years respectively.

Case 5,545 was 3 years old at the operation and showed, 2 years afterwards, no sign of recurrence.

Case 6,799 was 3 years old when operated upon and was reported alive 8½ months afterwards.

Case 6,834 was 3½ years when operated upon.

Case H.R.I. (*a*) was 3 years old when operated upon and was alive and well 17 years afterwards.

Between 3 and 6 years there are 3 cases to be recorded: Nos. 222, O.P., 5,802, 6,425. At 3½ years, 4½ years, and 5$\frac{11}{12}$ years respectively. The first case was operated upon when 4 years old and showed no recurrence 5 years afterwards. The second patient was 4½ years when operated upon and is alive and well 5$\frac{3}{12}$ years afterwards.

The third patient was 6 years old when operated upon. She was reported alive 6 months subsequently.

The above figures may be summarised as follows:—

Age at which growth was first noted.		Specimens, No. of.
At birth	0	Within 1 year, 11.
Within 1 month	1	
Between 1—2 months	3	
2—4 „	2	
4—6 „	3	
6—12 „	2	
1 year—1½ years	2	Within 1—3 years, 9.
1½—2	2	
2 —2½	1	
2½—3	4	
3 —4	1	Within 3—6 years, 3.
4 —5	1	
5 —6	1	
	23	(21 patients).

Recoveries and Duration of Life in non-Fatal Cases:—An attempt has been made to trace again several cases quoted in Mr. Marshall's paper. Many had already passed the three-year limit, which has been arbitrarily adopted as the time necessary to elapse before the patient is to be considered out

of danger. As a result of investigation, the figures below are obtained:—

No. 66.	Alive; no recurrence...	$13\frac{8}{12}$ years after operation.	
„ 68.	„ „ ...	$12\frac{11}{12}$	„ „
„ 69.	„ „ ...	$12\frac{7}{12}$	„ „
„ 71.	(double enucleation); no recurrence	$12\frac{1}{12}$ and $7\frac{2}{12}$	„
„ 72.	Alive; no recurrence...	$12\frac{1}{12}$	„ „
„ 74.	„ „ ...	$11\frac{11}{12}$	„ „
„ 78.	„ „ ...	$10\frac{7}{12}$	„ „
„ 83.	„ „ ...	$10\frac{2}{12}$	„ „
„ 86.	„ „ ...	$9\frac{4}{12}$	„ „

Of the unilateral growths:—

Case 69.—In November, 1897, this patient was reported to be "extremely ill, is delirious, and has convulsions." Mr. Marshall says, "it looks as if the period (three years) would have to be lengthened." The child, however, was alive and in good health in January, 1905.

Case 78.—Had just passed the three-year limit.

Case 83.—It was impossible to trace the patient when Mr. Marshall wrote his paper. Now, however, reported alive.

Case 86.—Had not passed the limit.

Of the bilateral growths:—

Case 71.—This was a double enucleation. It adds yet another case to his list of double enucleations (5 cases) who may be considered cured.

Case 84.—From a study of this case it would at first sight appear that the three-year limit was insufficient. The left eye was removed in February, 1895. In October, 1897, the child was in good health. The other eye, however, was seen to be involved. He died of a "lingering illness" on April 26, 1900, a period of five years after his original operation. The fact, however, we are dealing with a second eye must not be forgotten. Messrs. Lawford and Collins had 8 permanent recoveries. This figure includes one double enucleation. Vetsch gives 2 out of 25, Luke 5 out of 27.

With regard to recoveries and duration of life in non-fatal cases in the present series, observations must be limited for the most part to the 24 cases occurring in the actual practice of this hospital.

In January, 1905, 8 cases were reported alive.

They are:—

Case	5083	.....	8 years.
„	5123	.....	$7\frac{11}{12}$ „
„	5404	.....	7 „
„	5802	.....	$5\frac{3}{12}$ „
„	5966	.....	$4\frac{6}{12}$ „
„	6555	.....	2 „
„	6577	.....	$1\frac{10}{12}$ „
„	6799	.....	$8\frac{1}{2}$ months.

From these figures it is seen that 5 have passed the limit. They are all cases with unilateral involvement.

Cases 5,610, 6,834, were known to be alive 7–8 months and 2 months respectively after operation. They are in all probability dead, but the actual date of death cannot be ascertained.

Case 5,548 was reported alive in January, 1901 ($= 2\frac{4}{12}$ years after), but no reply was obtained to inquiries in January, 1905.

The subsequent history of 7 cases is quite unknown. Of the private cases, 3 have passed the limit.

222, O.P., known to be alive.....			$4\frac{1}{2}$	years	after operation.
H.R.I. (*a*)	„	„	6	„	„
H.R.I. (*b*)	„	„	6	„	„

Duration of Life in Fatal Cases.—Among the 24 hospital patients mentioned in this paper, 6 cases proved fatal. In 2 cases both eyes were involved. In addition to the 6, 2 are probably dead.

	Age at operation.	Died.
Case 5585	4 years	5 months after operation.
„ 5935	2 „	$6\frac{3}{4}$ „ „ „
„ 6248	7 „	$1\frac{5}{12}$ years „ „
„ 6425	6 „	6 months „ „
„ 6636	3 „	3 „ „ „
„ 6676	$1\frac{6}{12}$ „	$7\frac{3}{4}$ „ „ „

The intervals between the discovery of the growth in these cases and the operation are :—

Case 5585..... "Patient blind since 2 years old."
„ 5935..... $1\frac{1}{2}$ years' interval.
„ 6248..... Patient received injury 7 months prior to operation. Pain and swelling commenced 5 months after injury.
„ 6425..... 6 weeks' interval.
„ 6636..... 1 year interval.
„ 6676..... "Blind since 8 months old."

The corresponding figures in the non-fatal cases, for comparison, may be quoted here :—

	Age at operation.	Age when growth detected.	Interval.
Case 5083	$1\frac{10}{12}$ years	?	—
„ 5123	2 „	$1\frac{3}{12}$ years	9 months.
„ 5404	$1\frac{6}{12}$ „	2 months	$1\frac{4}{12}$ years.
„ 5802	$4\frac{1}{2}$ „	$4\frac{1}{2}$ years	—
„ 5966	2 „	No mention	—
„ 6555	$0\frac{1}{12}$ „	„	—
„ 6577	6 „	Just under 6 years	—
„ 6799	3 „	$2\frac{1}{12}$ years	1 month.
„ 6834	$3\frac{1}{2}$ „	$2\frac{9}{12}$ „	9 months.

The longest interval between operation and death, from these figures, is $1\frac{5}{12}$ (6,248). In this case an injury appears to have drawn attention to the state of the eye. The shortest interval is 3 months (6,636). All the patients who

are dead were over $1\frac{1}{2}$ years when the operation was performed. In Case 6,425 the disease apparently was only noticed six weeks prior to operation. In one non-fatal case an interval of 1 year and 4 months elapsed between discovery and operation.

Among the fatal cases in Messrs. Lawford and Collins' series, the longest interval between death and operation was 1 year 2 months (Case 2).

In Mr. Marshall's series the figure is $2\frac{2}{12}$ years (Case 70) if we exclude Case 84.

Site of Recurrence.

Definite statements with regard to this point are as follows:—

1. Case 5,585 — A swelling was noted in the orbit. It grew very rapidly.
„ 5,655 — The child died a few months after enucleation.

2. Case 5,610.—The left globe had been enucleated. There was a firm growth protruding from the lids 8–9 months subsequently. Actual date of death unknown.

3. Case 5,935.—The right globe had been enucleated, and the child died $6\frac{3}{4}$ months subsequently with large recurrence in the orbit. The end was ushered in with convulsions, and the patient died comatose.

4. Case 6,248.—The exenteration of the orbit was performed a few weeks subsequently to the primary operation. The child lived, however, as long as $1\frac{1}{2}$ years after the original operation.

5. Case 6,676.—In this case there was a *post-mortem*. Both orbits were full of glioma tissue. The anterior part of the scalp was infiltrated and thickened. The cranial bones and the chiasma were also involved. The inferior surfaces of the frontal lobes were pitted, but not involved.

6. Case 6,834.—Here exenteration was performed about 2 months after the primary operation. The socket was filled

with growth. The child complained of headache, and was vomiting. No secondary growths were detected. The subsequent history cannot be obtained.

7. Case 288, O.P.—In this case, 4 months after the original operation a recurrent growth was noted, as a growth over the nose. The second operation was performed 6 months after the original operation. The child died 11 weeks after the last operation.

The longest interval which elapsed between operation and recurrence in Messrs. Lawford's and Collins' cases was 9 months.

The intervals in the present series would appear to range from a few days to 8 or 9 months.

8. Case 456, O.P.—Recurrence was here noted at the apex of the orbit 1 month subsequent to primary operation. Exenteration was performed within a month from that date.

9. Case 654, O.P.—In this case, within 5 days recurrence was noticed. Exenteration had to be performed within a month of the primary operation.

On the Possible Shrinkage of Eyes.

No attempt will be made to discuss in this paper this important question. The reader is referred to the paper by Mr. Parsons, published in the Hospital Reports, vol. xvi, part 2. The whole question is there carefully considered, and a record of all such cases will be found. Suffice it here to say that one of the cases which tend to prove that glioma cells occur in shrunken globes is to be found in this present series, viz., No. 6,676. This patient is one of the 4 cases in which the tumour was bilateral. Mr. Parsons quotes full details of this case. The more important points, however, will be found in the tables.

In Case 5,610 we have to deal with a shrunken globe. In this case the left eye had been shrinking since 5 months old. A white spot had been noted on the right since the child was 3 months old. Microscopic examination showed small round cells and calcareous degeneration. The exact date of death

cannot be determined. In this case also both eyes were involved.

The left globe in Case 397, O.P. (a unilateral case) is reported to have been small and shrunken.

Temporary retrogression in glioma retinæ is stated to occur. In the present series of cases there would appear to be no grounds for proving or disproving the statement.

There is no evidence in favour of a spontaneous cure.

Family History.

It would appear that it is unusual for more than one member of a family to be afflicted with glioma retinæ. Messrs. Lawford and Collins in their paper say, "we have had no instance in which more than one member of the family has suffered from glioma of the retina" (Glioma Retinæ, Hospital Reports, vol. xiii, p. 21). Mr. Marshall in his article on this subject records the family history of one of his cases (Case 89) which is of extreme interest. A child, aged 2, had her right eye removed for glioma. At the operation the left eye was examined. It was found to contain a glioma. This eye was not removed; she died a few months later. The first child of this patient's family died at 2 years with convulsions; a white mass had been seen in the eye but no operation had been performed. The second child, a boy, died, aged 3 months, with convulsions. His eyes were not known to be affected. The third child, 15 years old in 1897, had an eye removed in Guy's Hospital. The appearance seen was similar to that seen in the first child's eye. The fourth and fifth children, aged 9 and 7 years, were both healthy and had no eye affection. The sixth is the patient, Case 89.

Mr. Marshall also quotes a case from Fuch's text book of Ophthalmology (p. 418), which is briefly as follows. The first child, aged 4, was a patient in which the right globe was removed. The growth had perforated the sclerotic. It died 6 months later. The second patient was a brother, aged

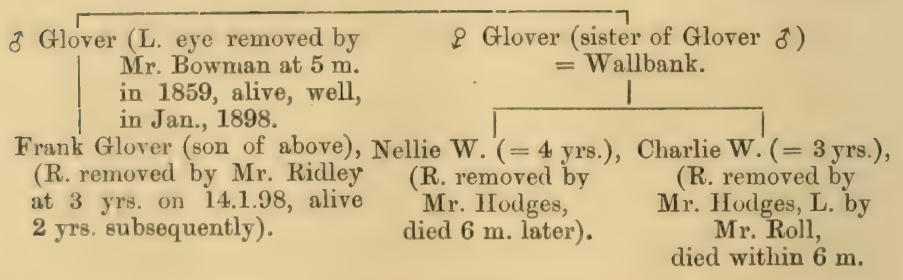
2 years. The patient's right eye was involved by a glioma. He died a year subsequently of a recurrent growth. The third child was brought for examination, but had only a coloboma of iris and choroid.

In the present series of cases the family histories are again of little or no import with one marked exception. For this case (211, O.P.) I am indebted to Mr. Ridley, who has kindly corroborated the details. Mr. Parsons in a clinical lecture upon glioma retinæ, delivered at the Great Ormond Street Hospital for children, says, "There is no case on record of a child from whom a gliomatous eye has been removed growing up and having children with glioma" (Clinical J., March 22, 1905). Mr. Ridley's case would appear to negative this statement.

The family history is briefly as follows:—A patient named Glover (a male) had his left eye removed for glioma, by Mr. Bowman, when 5 months old, in 1859. The diagnosis at this early date is, of course, open to doubt. He was reported alive and in good health in January, 1898.

The son of this man, Frank Glover (Case 211, O.P.) had his eye removed by Mr. Ridley on January 14, 1898, at the age of 3 years. "He was alive and well 2 or 3 years after the operation."

The sister of the first-named patient had two children. The elder, Nellie Wallbank, had the right eye removed when 4 years old, for glioma, by Mr. Hodges. She died 6 months later. The second child, Charlie Wallbank, had both eyes involved and died very shortly after the second eye had been removed. The family tree is as follows:—


♂ Glover (L. eye removed by Mr. Bowman at 5 m. in 1859, alive, well, in Jan., 1898.
♀ Glover (sister of Glover ♂) = Wallbank.
Frank Glover (son of above), (R. removed by Mr. Ridley at 3 yrs. on 14.1.98, alive 2 yrs. subsequently).
Nellie W. (= 4 yrs.), (R. removed by Mr. Hodges, died 6 m. later).
Charlie W. (= 3 yrs.), (R. removed by Mr. Hodges, L. by Mr. Roll, died within 6 m.

Many other authorities quote cases in which more than one member of the family were afflicted with glioma. Among these may be mentioned, v. Graefe, Calderine, Newton, Lerche, Sichel, Fuchs, Wilson. In one of Wilson's cases 8 children in one family were afflicted. The following remarkable family history of a case of Newton's is taken from the *Lancet* of November 22, 1902, being a quotation from the *Australian Gazette*. The patient, aged 2, was quite blind, having each eye occupied by a growth. She was the youngest of a family of 16. Of these 2 died in infancy from bronchitis—4 alive and well; 10, including the first-named patient, died of glioma; none lived beyond 3 years except one. That patient was operated on for unilateral growth and died aged 5. There were 3 unilateral and 7 bilateral cases. The eyeball ruptured in every case except one. The sexes were equally divided. An uncle in this family is said to have died in infancy with an eye complaint, the nature of which is not stated.

In the face of such evidence as this we may conclude that although, in the vast majority of cases, glioma only attacks a single member of a family, yet there is plenty of evidence to show that many members may be attacked.

It is, however, extremely rare for a patient with glioma subsequently to have a child who also develops it. It is presumably a family not a hereditary disease.

In conclusion I beg to offer my especial thanks to the following gentlemen:—To Mr. Herbert Parsons, for permission to study the museum reports and specimens, and for much valuable assistance. To Mr. Coats, for many kind suggestions. To Messrs. Rockliffe and Ridley, for the great trouble they took to furnish particulars, and corroborate the details of their cases.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
1 5083	Richard Bird Mr. Tweedy 5.1.97	?	?	$1\frac{10}{12}$	8 yrs.	None	T. +
2 5123	Rose Babir Mr. Silcock 26.2.97	L.	8 or 9 m. ago "white appearance; red last 5 wks."	2 yrs.	$7\frac{11}{12}$	None	T. +
3 5299	Eva Wayth Mr. Lang 30.9.97	L.	"5—6 wks. ago; seemed to grow v. rapidly after first noted; apparently painless."	12 wks.	...	...	T. + 2

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Conjunctiva œdematous; cornea steamy; contents of A.C. appear blood-stained; pupil dilated. *Section.*—Lens displaced back. Vitreous occupied by large solid mass; loose, friable, nodulated; colour: dirty white; mass occupies two-thirds of globe; remaining one-third filled with loosely coagulated albuminous material. *Micro.*—A.C. deep. Angle quite obliterated. Iris displaced back. O.N.: intra-ocular part involved, but extra-ocular not; nerve cut long. Growth springs apparently from posterior pole of eye.	No mention	10.1.05 no recurrence.
Cornea, lens, clear; A.C. normal; large yellowish mass to be seen behind lens; seems to have blood extravasated on surface. *Section.*—A.C. normal in depth; angle quite closed by adhesions between iris and cornea. Lens *in situ*. Vitreous: two-thirds occupied by large glioma, which is covered with hæmorrhages. It extends over two-thirds of retinal surface. Portion runs forward in hyaloid canal. O.N. cut very short indeed. *Micro.*—Ant. angle closed by adhesions. Iris somewhat atrophied. Ectropion of uveal pigment. O.N. apparently involved. Growth springs from vitreous surface of retina; glioma endophytum. Much degeneration.	Mother healthy; no miscarriages. Three children by first husband, one (the patient) by second. —— No previous history of eye affection in children.	L. eye never inflamed; R. eye apparently healthy. January, '05 alive, well.
Cornea hazy; A.C. shallow; large growth seen in eye. *Section.*—Angle A.C. closed; iris and cornea in contact. Lens pushed forward to back of iris. Globe filled three-quarters with solid glioma. Retina, where recognised, entirely detached. Running from optic disc to back of retina is the central artery. Choroid much atrophied. *Micro.*—Growth much degenerated. Cells are of small, round variety; vascular in parts.	Father healthy; parents not blood relations. Patient is second child; elder child, 18 months, healthy. No F. H. of eye affection.	Written to January, '05. No reply.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
4 5383	Arthur C. Outen Mr. Tweedy 25.1.98	R.	White mass; seen 1 yr. ago. No notice taken till 6 wks. ago.	$3\frac{2}{12}$	$7\frac{1}{3}$ yrs.	None	T. n.
5 5404	Daisy Lovegrove Mr. Lang 21.2.98	R	First noticed when 2 m.	$\frac{10}{12}$	7 yrs.	...	T. +
6 5545	Douglas Vincent Mr. Lawford 10.9.98	R.	White spot detected 8 wks. ago	3 yrs.	...	...	T. n.

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
A.C. (?) shallow. White floating mass seen. *Section.*—A.C. normal in depth; iris healthy; lens *in situ*. Vitreous: About four-fifths occupied by partially detached retina; from inner surface of which grows large diffuse gliomatous-looking mass. Whole retina involved; it is thickened; on one side mass nearly extends up to the ant. posterior diameter. Choroid not involved. O.N. cut long; not swollen. *Micro.*—Angle of A.C. narrow, but open; no evident iritis or cyclitis. Retina: detached, thickened, thrown into folds. Growth shows much degeneration, also small round cells, identical with ordinary exudation cells. O.N. apparently quite unaffected.	Father and mother healthy. No consanguinity. One child died æt. 1 year. Patient is eldest child.	Patient had trouble with eyes during first week of life, viz., profuse discharge. Recovery within 3 weeks. Nothing noticed until 1 year ago. Patient has never complained of the eye. — May, '05. In good health. Socket normal. L = 6/6 vision.
Cornea hazy. Eye enlarged. Vertical = 13·5 mm. Ant.-Post. = 24·5 mm. Transverse = 22 mm. *Section.*—Ant. chamber normal depth; angle closed; lens *in situ*; choroid *in situ*. Vitreous entirely filled with large tumour; partly opaque, partly transparent; only little degeneration; vessels and vascular spaces seen. Retina invisible. *Micro.*—No report.	Patient is eleventh child. One died 8 months old (lung trouble). Rest healthy. No eye affection.	Child never appeared to suffer much pain. L. eye apparently healthy. Alive 20.2.05. Socket normal. L. normal.
Anterior part eye apparently healthy. Yellowish mass can be seen in lower vitreous. *Section.*—Cornea clear; ant. chamber normal; angle open; lens clear, *in situ*. Vitreous chamber much diminished in size owing to large tumour; soft; vascular, flocculent; whitish-yellow in colour; tinged with hæmorrhages interiorly; shows much degeneration. Growth reaches from back of iris to point just posterior to equator of globe. Retina: greater part *in situ*, except at anterior part, where it is detached with choroid. Shows outlying nodules.	Nothing stated ...	16.1.01. No sign recurrence. L. eye healthy. Not heard January, '05.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
5545	Douglas Vincent —*continued.*						
7 5585	Arthur Stanton Mr. Lawford 27.10.98	L.	L. been blind 2 yrs. Painful for 6 wks.	4 yrs.	...	...	T. +2
5655	Mr. Lawford 15.2.99	...	...	5 yrs.	5 m.	3 wks. ago swelling noticed in orbit. Has grown very rapidly.	...
8 5610	May Wallis Mr. Silcock 2.12.98	L. and R.	L. been shrinking since 5 m. old; white spot noticed in R. since 3 m. old.	2 yrs.	?	...	Not mentioned.

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
O.N. not obviously affected; is cut off flush with sclerotic. *Micro.*—Small round cells; patchy areæ of degeneration; growth springs apparently from extreme inner surface of retina; greater part of retina appears healthy.		
Eye very much enlarged. Cornea hazy; eye apparently full of growth, yellowish in colour. Annular staphyloma in ciliary region. O.N. much enlarged. *Section.*—Sclerotic, much stretched, thinned, especially in ciliary region. Iris much displaced to each side, so that it forms part of the ciliary staphyloma. Lens pushed forward; in contact with back of cornea. Remainder of globe filled with large gliomatous mass; consists of two parts, inner and outer; former is in vitreous chamber, much degenerated; has calcareous appearance, bounded externally by choroid; sharply limited from rest of growth; latter composed of more recent tissue; is translucent; has numerous small degenerated areæ. Several small hæmorrhages. Lamina cribrosa has given way. Growth continued along optic nerve, which is entirely occupied by glioma cells. Growth must have extended very far back.	No mention.	
Contents of orbit removed, but not completely. Stump could not be removed. *Micro.*—Typical glioma, with much degeneration.	. .	Patient died 31.3.99.
L. globe much shrunken; nothing can be seen owing to blood in A.C. *Section.*—Sclerotic; cornea, much thickened; shrunken. Iris hardly distinguished. Vitreous absent. Retina cannot be distinguished. Choroid somewhat detached. Interior globe solid with dense material containing numerous calcareous nodules.	No mention	No reply January, '05.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
5610	May Wallis—*continued.*					25.7.99. L. lids protruding with twin growth. Child wasting rapidly; appears to be in great pain.	...
9 5639	Ella Kitchener Mr. Spicer 11.1.99	R.	White mass 3 m. ago. Been increasing last 4 wks.	$1\frac{1}{12}$	...	...	No mention.
10 5802	Grace Combes Mr. Gunn 7.10.99	R.	14 days ago something noticed in front of eye.	$4\frac{1}{2}$	$5\frac{3}{12}$ yrs	...	T. full

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Micro.—Small round cells; calcareous degeneration; whole eye involved; no structure recognisable; cannot say where growth commenced. 25.7.99. R. pupil widely dilated; yellow reflex.		
White mass to be seen in vitreous. Lens, cornea, clear; A.C. normal. *Section.*—A.C. normal; angle open. Lens normal, *in situ*. Large glioma situated on nasal side of eye. Shows typical degenerated patches. It covers the optic nerve. Choroid, *in situ*. Sub-retinal space filled with albuminous material. O.N. divided far back. Impossible to say if nerve is involved. *Micro.*—Anterior eye healthy; large glioma grows from nasal retina; much degenerated. Choroid not involved. O.N. involved near ocular end. Shows much cell proliferation.	Father, mother, healthy. No consanguinity. Patient youngest of 10. Seven still alive. Third and sixth died (lungs), eighth cross-eyed, since wh. C.	There has been discharge from ears 6 months. No fits. No reply January, '05.
Grey opacity to be seen; shakes on movement of eye; surface irregular; shows hæmorrhages; eye normal to external appearances. *Section.*—Anterior angle slightly restricted; lens much flattened; clear. Flocculent white mass occupies fully three-fourths of interior of globe; typical degenerated areæ. Retina intact, but infiltrated with growth, dense and white. O.N. cut only 3·5 mm. from retina. Much infiltrated with growth. *Micro.*—Anterior eye healthy; angle A.C. narrow; vitreous occupied by large glioma, which grows from retina; unaffected retina thickened; choroid *in situ*. O.N. infiltrated up to point of section.	No mention	Alive 28.1.05. L. eye normal.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
11 5935	May Johnson Mr. Lawford 9.5.00	R.	R. wrong since 6 m. old.	2 yrs.	$6\frac{3}{4}$ m.	Large recurrence in orbit. Patient died with convulsions and comatose.	T. +1
12 5966	E. May Gowling Mr. Morton 10.7.00	R.	No mention	2 yrs.	...	...	No mention.

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
A.C. now deep; pupil dilated, oval, long axis horizontal. Yellowish white reflex from back lens. Yellowish growth seen protruding through centre of O.N.	Patient one of three living. Two (twins) died at 6 and 9 months.	Before operation. R. deviates in. Cornea clear. A.C. shallow.
Section.—Iris adherent at angles to cornea. Lens shrunken; pulled back from iris. Retina detached; from it springs white flocculent mass extending into vitreous and into subretinal space. Surface choroid involved, but is *in situ;* O.N. involved.		Pupil immobile, dilated, regular. Large white mass seen; irregular flocculent. No red reflex. No P.L. Left cornea clear.
Micro.—Retina greatly degenerated. Various layers not to be differentiated. In most parts one thick layer of deeply-staining nuclei is visible. Growth chiefly endophytic; shows much degeneration; spreads forwards along hyaloid membrane from ora serrata to back of lens. O.N. shows growth occupying its centre with small amount of apparently degenerated fibres round margin.		Good A.C. Pupil active. Fundus not examined. Father thinks child has had pain. Died 30.11.00.
A.C. shallow. Iris clear; no retraction at base; whitish-yellow reflex—more or less irregular three-lobed appearance, in which some blood-vessels are seen. *Section* (Horizontal).—Eye nearly full of white flocculent growth. A.C. nearly obliterated. Lens, yellow, misshapen. Posterior surface drawn back into peak at point where retina passes back to O.N. Retina detached; seat of growth; choroid *in situ;* O.N. apparently not infiltrated. *Micro.*—Shows exophytic growth. At one spot layers of retina seen to be involved. Growth seems to spring almost entirely from inner nuclear layer. Inner G. layer invaded also G. and N.F. layers. Eventually comes to lie next to vitreous. No rings of cells. Cells grouped round blood-vessels. Little degeneration only.	F. labourer ..... Other children healthy. No eye affection.	Before operation. Three-lobed yellowish mass seen by oblique illumination. Alive, well, 28.1.05. Good health since operation. Left eye examined by medical man. Said to be normal. R. socket healthy.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
13 6248	Maddie Widdick Mr. Gunn 12.10.01	R.	2 m. ago pain, swelling commenced. Pain in eye 7 m. ago; became bloodshot.	7 yrs.	$1\frac{6}{12}$ yrs.	...	No mention.
6248A	23.10.01	...	...	...	...	Recurrence in orbit. R. orbit exenteration, 23.10.01.	...
14 6425	Amy Sylvester Mr. Morton 29.7.02	L.	L. noticed different from R., 6 wks. Pain at times.	6 yrs.	...	...	T. ? >R.

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Globe fully twice normal size. Lobulated growth on nasal side. O.N. cut long, but obviously much enlarged; infiltrated with growth. *Section* (Horizontal).—Globe filled with lobulated growth, only lens, cornea, with parts of sclerotic to be distinguished. O.N. much swollen; gelatinous; infiltrated. Large mass of growth stretches forward from disc to lens. *Micro.*—Section of posterior pole shows well-marked intra- and extra-ocular glioma. Central mass grows forwards from disc. On each side is a mass sharply cut off which replaces choroid. It is covered with normal lamina vitrea and normal retinal pigment epithelium. Growth atypical glioma with large eosine staining degenerated areæ. Some areæ show well-marked pigmentation. Increase in O.N. due to large sheath of growth; true nerve being degenerated. Lids and orbital contents:— Lachrymal gland and O.N. hard. Other tissues seem normal; L. gland inflamed, invaded with leucocytes. Nerve at back of orbit surrounded with large mass of growth. Glioma probably already intracranial.	No mention	Before operation. Has had headache, giddiness for 2 months. Vomiting nearly every day for 3 weeks. R., considerable proptosis. Nasal side swollen, lobulated. Cornea rotated out, opaque. L., pupil reacts.
	...	Death, 26.4.03, "from the effects of her eye."
Left cornea now clear. ? haze due to tension. White flocculent coagulum in lower part A.C. One small round mass readily moves about in aqueous. White material seen in fundus. *Section.*—Cornea good. A.C. good. Globe nearly filled with white growth. Retina can only be traced in places. Choroid invaded below. O.N. invaded. *Micro.*—A.C. normal. Both angles blocked by adhesions of iris to cornea. Flocculent mass in lower angle consists of cells of varying size, shape; also pigment granules. Iris normal. Vitreous full of glioma; shows comparatively little degeneration. Typical columns and ring cells arranged round blood-vessels.	Phthisis in family	Before operation. L., cornea hazy. A.C. shallow. Pupil dilated; inactive. Iris vascular. Yellow-greyish reflex. Large irregular nodular masses with considerable vascularity. No tenderness. R., cornea clear. Iris normal. Fundus normal. Died 25.1.03.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
14 6425	Amy Sylvester — *continued.*						
15 6536	Lily Gourd Mr. Spicer 7.1.03	R.	No mention	3 yrs.	...	...	No mention.
16 6555	Bertram Mulloch Mr. Lawson 23.2.03	L.	No mention	$\frac{9}{12}$	...	...	No mention.
17 6577	Bella Nisbet Mr. Spicer 28.3.03	L.	12.3.03. Vision in L. found defective. 14.3.03. O.P.	6 yrs.	$1\frac{10}{12}$ yrs.	...	T. full.

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Growth entirely endophytic. O.N. infiltrated with growth anteriorly. Cut end and posterior 3 mm. are normal.		
Section (Down and out).—Cornea; A.C.; iris; lens; all normal. Large grey, dead-white tumour situated on outer side; grows from retina. Base = 11 mm. Thickness = 13 mm. Front of base is 4 mm. from angle of A.C. Growth nearly touches back of lens. Has very white patches on it, characteristic of glioma. Unusually isolated for a glioma; no visible satellites. Growth far from nerve. Remaining retina *in situ*. One wavy distended vessel passes from disc on to tumour. Choroid is *in situ*. *Micro.*—Glioma endophytum; no rings; no satellites. O.N. normal.	No mention	Before operation. R., cornea clear. A.C. good. Iris normal; no retraction at periphery. White glistening nodular mass in vitreous on outer part. L., normal.
Section (Sagittal).—A.C. shallow. Vitreous full of glioma; no evidence of extra-ocular extension. *Micro.*—A.C. shallow; angle blocked. Glioma fills globe. Chiefly endophytic; much degenerated.	No mention	Before operation. 16.2.03. L., A C. very shallow. ? glioma. 21.2.03. L. > R. Cornea clear. A.C. shallow. Pupil smaller than R. Iris discoloured. White opaque mass behind pupil. January, '05. Alive, well. Socket said to be healthy by medical man.
Section (Down and in).—Glioma forms thick cap inside posterior part of sclerotic; many hæmorrhages. Cornea very slight œdema. A.C. one angle. *Micro.*—Compact cellular tissue, and very early adhesions of iris. Iris normal. Lens shows early peripheral changes. Retina almost entirely gliomatous (endophytic). Choroid not involved. O.N. involved near disc. Cut end normal.	No mention	Before operation. 24.3.03. L., no retraction of iris at periphery; dull brown; reacts consensually. Nodular mass projects into vitreous, down and in. R., iris bright, grey. T. n. Alive, well, 28.1.05.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
18 6636	May Moore Mr. Morton 11.8.03	R.	Coming on 12 m.	3 yrs.	3 m.	...	T. +
19 6658	Thomas Martingale Mr. Fisher 19.9.03	R.	White reflex noticed 15.9.03.	$\frac{9}{12}$	...	...	T. n.
20 6667	Ellen Hellyer Mr. Lang 28.9.03	R.	Has squinted 6 m.	1 yr.	...	...	No mention.

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Globe and orbital contents:— A.C. deep; angles adherent. There are pearly points; degenerated areæ. Retina extensively involved. Growth just external to O.N. is extrascleral. O.N. sheath involved. Vaginal space filled with tumour tissue. *Micro.*—Cornea with epithelium gone; œdematous. Pus shows peripheral anter. synechiæ each side. Ectropion uveal. Lens cortex largely homogeneous. Ciliary body degenerated. Postero-ext. part involved. Globe nearly full; much degenerated glioma. Choroid largely replaced by glioma. O.N. head involved, also posterior part near cut end. Large extra-ocular growth behind.	No mention	Influenza Easter. Before operation. R., no injection. Proptosis. Cornea clear Green reflex. T. +. L., normal. Died 10.11.03.
Section (Sagittal).—A.C. shallow; iris normal; also lens. Retina completely detached, especially below. Choroid: white over whole lower part, with sharply defined edges. ? coloboma. *Micro.*—Cornea normal. A.C. shallow. Angles open. Lens: cortex cataractous. Retina completely detached; glioma exophytum. Choroid shows nodules on inner surface. No coloboma.	No mention	Before operation. R. A.C. shallow. Iris bright. Lens clear; yellow irregular mass with vessels over it. L. normal. No reply January, '05.
Section (Horizontal).—A.C. contains blood. Iris has white nodules near pupil. Lens *in situ*. Retina detached—trumpet shaped. Large mass of glioma round disc. Many satellites behind retina and on choroid; latter degenerated. *Micro.*—Cornea: some œdema. A.C., angles full of glioma, which also extend along back of cornea. Hyphæma. Iris covered and involved; lens degenerated. Ciliary body a mass of glioma. Choroid involved. O.N. much degenerated. Anterior part full of growth.	—	Before operation. R. chemosis. Cornea hazy. Pupil dilated; old hæmorrhage. Greenish-white reflex. L. normal. No reply January, '05.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
21 6673	Ellen Hooper Mr. Collins 5.10.03	R.	23.7.03. R. eye struck 6 wks. ago by corner of chair; became inflamed.	3 yrs.	...	...	T. n. or +
22 6676	Edith Hopping Mr. Gunn 7.10.03	R. and L.	Blind since measles at 8 m., and eye usually kept closed since pneumonia 6 wks. ago.	$\frac{1}{12}$	...	12.3.04. Recurrence in R. socket. 6.10.04. Contents of R. orbit protruding through palpebral fissure in fungating mass.	T. –

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Section (Sagittal).—A.C., one angle blocked. Lens *in situ*. Retina detached; extensive glioma exophytum. Choroid *in situ*; no visible deposits. O.N. infiltrated in anterior part. *Micro.*—Both angles A.C. blocked by peripheral anterior synechiæ. Glioma cells in lower angle. Iris. Ectropion uveæ. Cil. body degenerated. Choroid not affected. No nodules on surface of Bruch's membrane.	Two other children healthy	Before operation. R. A.C. shallow. Iris pushed forward, discoloured; fine vessels on it below. Pupil well dilated. Yellow-white reflex; vessels on surface below. L. normal.
Right globe: shrunken. Antero-posterior = 16 mm. Transverse = 18 mm. Vertical = 16 mm. *Section* (Sagittal).—Cornea very thick. A.C. absent. Iris pushed forward. Lens, large cataractous. Behind lens is yellowish-white mass with reddish spots on it; uveal pigment surrounds it. *Micro.*—Cornea: epithelium thin, ill-formed; Bowman's membrane v. wavy. Subst. Propria much thickened, vascularised, œdematous. Descemet wrinkled; endothelium present only in places; microscopic deposit of pigment. A.C. small, irregular. Iris is transformed into hyaline fibrous tissue, with pigment in meshes—horizontal long rod-shaped nuclei—is adherent everywhere to capsule of lens. Lens cataractous. Ciliary B. detached posteriorly; much degenerated. Choroid: congested, degenerated; condition is characteristic of phthisis bulbi. Retina cannot be recognised, except pigment cells. Internal to choroid is layer of new formed connective tissue; irregular in thickness; greater everywhere than that of underlying choroid. Tissue vascular; highly cellular. Spindle cells and asteroid cells with long nuclei. Outer boundary formed by nearly continuous coal black pigment epithelium (retinal).	Four other children. No miscarriages. All good sight.	Before operation. R. much shrunken, much infected. Cornea hazy. A.C. shallow. Iris bluish-green, vascular. Lens ? opaque. Fine vessels run on to capsule. No reflex. T. −. L. cornea clear. A.C. shallow. Iris discoloured, vascular. Yellow reflex. Hæmorrhages. T. n. 12.3.04— L. eye full; œdematous. Conjunctiva protruding. elastic swelling to be felt. Cornea enlarged. Iris discoloured. Yellowish reflex behind clear lens. 6.4.04— L., marked proptosis; fungating mass above, below. Cornea dry, ulcerated. 8.4.04— L. eye proptosed and perforated. 30.4.04. Death. For full description and discussion on shrunken globes, *vide* O. H. Rep., vol. xvi, pt. 2. "Case of great importance as an almost incontestable

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
22 6676	Edith Hopping —*continued.*						
23 6799	Caroline Newman Mr. Lawford 14.5.04	R.	R. noticed different from L. 2—3 wks. Measles followed by pneumonia 12 m. ago.	3 yrs.	8½ m.	...	T. + 1.
24 6834	Lazarus Wineberg Mr. Gunn 18.6.04	L.	27.9.03 Small red spot noticed. Violent retching day before commencement.	3½	...	22.8.04. Socket filled with growth in last fourteen days. Child complains headache — no vomiting, no secondary growths detected.	...

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Vitreous: whole cavity filled with granular material, staining with eosine; this composed of degenerated cells. O.N. atrophic, highly cellular. Cell nuclei vary greatly; most oval, faintly staining; probably neuroglial; others rod-shaped, deeply staining, of connective tissue origin; others small, round, deeply stained, probably gliomatous. Orbital intra-cranial extensions show typical features of glioma retinæ as it occurs in extra bulbar extensions. *Post-mortem* note. Head only examined:—Both orbits full of gliomatous tissue. Anterior part of scalp infiltrated and thickened; also cranial bones, chiasma. Roofs of orbit raised. Inferior surface frontal lobes pitted, but not involved.		case of glioma in a shrunken globe."
Section.—A.C. good. Lens shows changes. Retina: large mass of glioma in posterior part. Choroid *in situ.* *Micro.*—Not given.	Three other children alive.	Before operation. R. cornea hazy. A.C. good. Pupil dilated. ? Mydriatic. Does not react. Iris dull, vascular; Yellow reflex with white nodular streamers. No vessels or hæmorrhages seen. L. normal. Reported alive, well, 30.1.05.
Section.—A.C. absent. Lens cataractous; in contact with cornea. Retina forms large antero-posterior band of glioma. Choroid *in situ;* full of secondary nodules; larvæ ciliary staphyloma below. *Micro.*—Not given.	...	Progress of case. 3.10.03 = O.P. L. hyphæma (started as small red spot 1 week previously. Violent retching on previous day). 10.10.03. L. paracentesis. Iris discoloured, tremulous; yellow reflex from movable mass in vitreous. 18.6.04. L. ciliary staphyloma below. Cornea hazy. No A.C. Iris irregular, dilated, discoloured. Lens opaque. No reflex.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
24 6834	Lazarus Wineberg —*continued.*						
25 211	Frank Glover Mr. Ridley's case 14.1.98	R.	Mass noted 6 m.	3 yrs.	...	...	No mention.
26 222	Jessie Wright Mr. Rockliffe's case April, '98	?	6 m. ago.....	4 yrs.	...	...	?
27 244	? name, sex Mr. Lang's case June, '98 Middlesex Hospital	?	?	?	...	...	?
28 288	Charles Beniston Mr. Ridley's case 21.1.99	L.	At 12 m. ...	$1\frac{8}{12}$ yrs.	approx. 9 m.	At 2 yrs. age growth over nose remarked (secondary). $2\frac{2}{12}$ yrs. removed. Death 11 wks. after.	?

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
		22.8.04. See p. 34. R. is normal. 24.8.04. Exenteration L. orbit. Jan. '05, no reply.
A.C. almost obliterated. Retina entirely detached. Growing from outer surface is diffuse mass. *Micro.*—Cornea, iris, adherent; much atrophied; angle A.C. closed. Cil. body much atrophied. Difficult to say from which surface retina growth originates; probably outer; all appearances of glioma retinæ. O.N. head involved; ? the rest.	Family history very interesting:— ♂ Glover (L. eye removed in 1859 at 5 m. by Mr. Bowman, alive, well, Jan., '98. ♀ Glover = Wallbank. Nellie (= 4 yrs.), (R. removed by Mr. Hodges, died in 6 m. after op.) Charlie (= 3 yrs.), (R. removed by Mr. Hodges, L. by Mr. Roll, died in 6 m. Frank Glover (son of above), R. removed by Mr. Ridley, æt. 3 yrs., on 14.1.98. "Alive and well a year or two after." — Mr. Ridley.	
A.C. normal depth; angle open. Vitreous three parts full; large white growth. O.N. enlarged; semi-opaque. *Micro.*—Tumour a glioma, arising apparently from choroidal surface of retina. Growth v. extensive. O.N. much involved. Growth extends beyond point of section.	?	Child healthy. No recurrence March, '03.
Section.—A.C. normal depth; angle seen open. Vitreous two-thirds filled with dense white growth; numerous areæ of degeneration. O.N. obviously involved. *Micro.*—Typical glioma. O.N. involved to cut end.	?	
Cornea clear; A.C. shallow; angle appears closed; vitreous absent. Retina for most part cannot be recognised; detached; rest involved in large glioma; dense white colour; shows much degeneration. *Micro.*—Small round-celled glioma.		

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
29 328	? name ? sex Mr. Morton's case June, '99	?	?	?	...	...	?
30 335	—— K. ? sex Mr. Tweedy's case July, '99	?	First symptom noted when 2 m. Detached retina noted July 6. Enucleation 9.7.99. Exenteration 20.8.99, by Mr. Horsley.	3 m.	...	...	?
31 342	? name Mr. Ridley's case Sept., '99	...	...	...	...	...	?
32 358	? name Mr. Spicer's case 1900	?	?	?	?	...	?
33 397	—— M. Mr. Nettleship Nov., '00	L.	White reflex with vessels seen by father 3 or 4 wks. after birth.	Infant	...	...	T. −.
34 412	Grace S. Mr. Morton's case Jan., '01	L.	?	?	...	...	?

Ophthalmic Hospital. 1897–1905.

Summary of Curator's Report.	Family history.	Remarks.
Front part eye apparently healthy; vitreous two-thirds full large growth, which is whitish on surface. Pigmented and degenerated in parts. O.N. at point of entrance much enlarged. *Micro.*—Glioma. O.N. much enlarged.	Parents ♂.	
Eye examined by Mr. Lister: "It is glioma of retina." O.N. involved.	Father a medical man.	
Micro.—Recurrent glioma R.		
Retina seems to be studded with discrete white mould-like gliomatous growths. *Micro. Section* through ora serrata, shows thickening in external and internal nuclear layers. Whole retina involved in growth.		
Eye small, shrunken. Globe contains a very friable white substance. Retina appears detached. Cornea opaque. *Micro.*—Growth a glioma R., much degenerated. Difficult to say whether endophytic or exophytic. Shows rings of columnar cells. Probably chiefly endophytic. O.N. apparently not involved.	Father a medical man.	At 7½ weeks eye rapidly inflamed, swollen, chemosis; went down in few days. L. cornea semi-opaque. T. – somewhat.
Eye small. A.C. absent. Lying external to retina is large whitish growth, mottled on surface, choroidal surface covered over with white ivy-like growth for considerable extent. *Micro.*—A glioma. Growth involves nerve-fibre layer as if it were grown from this layer. O.N. not involved.	?	

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
35 420	? name Dr. Milligan's case Feb., '01	?	?	?	...	...	?
36 425	Arnold L. Mr. Bullar's case 28.2.01	R. and L.	March, '00. Something wrong with R. 2 m.; under homatropine a dislocated white lens; L. media clear. May, '00, began to go.	1½ yrs.	...	...	...
37 456	George Smith Mr. Rockliffe's case 7.3.02 Shown Ophth. Soc. 30.4.02 *Vide* Appendix Vol. 22	R.	...	3 yrs.	...	Recurrence first noticed 7.4.02. at apex of orbit. Apr. 22, size of walnut. Apr. 28, double in size. May 3, exenteration.	...
38 477	? name Mr. Lawson's case June, '02	?	?	?	1 m. or under.	...	...

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Micro.—Cornea N. A.C. angle closed. Vitreous absent. Retina detached. Glioma fills practically whole globe. Choroid normal. Glioma has a spread through coats of eye, and is invading orbit.		
L. A.C. deep. Lying under choroid, and infiltrating both choroid, retina, iris, cil. body, and extending into A.C. is white growth. O.N. much sunken and infiltrated. *Micro.*—Growth v. cellular; contains numerous blood-vessels. Cells large, round. Retina cannot be recognised. Growth infiltrates cornea and sclerotic.	...	February, '01. Left began to go wrong in May, '00. Child taken to Moorfields, where both eyes were said to be getting bad. Now L. much swollen, and A.C. full of yellowish substance. R. similarly affected, but to less degree. 28.2.01. L. enucleation (mass at back of orbit could not be removed).
Section.—Cornea N. A.C. normal. Ditto iris. Vitreous disappeared. Retina replaced by glioma, which fills globe from O.N. to back lens. *Micro.*—Angles obliterated. Lens invaded. Globe full of glioma. Layers of retina cannot be distinguished. Many areæ of degeneration in front. O.N. involved whole length. 5.5.02. Recurrent growth has replaced entirely the normal tissues, except portions of sheath and supporting tissue.		
A.C. good. Iris, cornea, lens, normal. Vitreous has delicate transverse membrane from which white threads pass back to retina. Retina extensively detached, much swollen. Nodules are white in section, with beautiful radiating streaks of hæmorrhages. O.N. looks normal. *Micro.*—A.C. good. Angles blocked. Retina, largely replaced by glioma, much degeneration; endophytic. Choroid infiltrated at posterior pole. O.N. seat of large degenerated mass just behind lamina cribrosa. Infiltrated to cut end.	?	Patient died July.

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
39 482	Madelein S. Mr. Lawford's case 24.6.02	L.	?	?	...	...	...
40 494	Peggie de K. Mr. Lang's case ? date	...	...	...	...	...	...
41 541	? name Mr. Sinclair's case 16.5.03	...	...	...	...	...	...
42 542	? name Mr. Maddox's case 20.5.03	...	...	...	...	...	...
43 595	John C. Mr. Lawford's case 6.5.04	...	...	$3\frac{6}{12}$	...	...	...
44 644	Victor A. Mr. Fisher's case 1.2.05	...	...	$1\frac{9}{12}$ yrs.	...	...	...

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Section.—Cornea, A.C., lens, normal. Retina gliomatous—one large growth (7 mm.) at inner part. Shows areæ degeneration. Rest of retina studded everywhere with nodules. Many isolated. Choroid apparently normal. O.N. short; looks healthy. *Micro.*—Glioma with neuro-epithelial rings.		
Micro.—Cornea normal. A.C. good. Iris, lens normal. Tumour, calcareous. Glioma, typical, with neuro-epithelial rings. Shows much degeneration. Covers disc, but does not extend quite as far as lamina cribrosa. A.C. angle blocked by peripheral anterior synechia. Iris degenerated; denser than normal. Lens distorted; changes chiefly at Equator. Retina detached; shows nodules of glioma; not far advanced. Glioma cells occur on pigment epithelium. Choroid unaffected. Ant. chamber angle blocked by peripheral anterior synechia. One angle contains small mass of glioma. Iris covered with thin layer of glioma. Globe filled. Choroid apparently normal. O.N. swollen; infiltrated for 2 mm.; normal beyond. *Micro.*—A glioma.		
Micro.—A glioma.		
Typical glioma macroscop.		

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
45 650	? name Mr. Worth's case 10.2.05	...	...	...	...	...	...
46 652	? name ♀ Mr. Marshall's case 4.2.05	R. + L. Both removed.	...	$\frac{11}{12}$ m.	...	...	...
47 H.R.I. 211 (α)	H. Bolton Mr. Rockliffe's case 3.12.81	L.	First noticed July, '81.	3 yrs.	...	...	T. n.
48 H.R.I. (β)	Rose Addy Mr. Rockliffe's case July, '93	R.	...	4 yrs.	...	...	...
49 H.R.I. 654 O.P.	Alice Blummilt Mr. Rockliffe's case 7.3.05	L.	Mother states from infancy.	$3\frac{1}{2}$ yrs.	...	Recurrent growth noted 12.3.05. Proptosis $\frac{3}{4}$ in. on March 31; exenteration.	T. + ?

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
Glioma exo.		
Cornea normal. Iris and corneo-iridic angle normal. Near ora serrata a small glioma-tous nodule showing typical necrosis. Nuclei around vessels. Rosettes. Some polymorpho-nuclear invasion. At edge of tumour all retinal elements seem involved. Rods and cones fairly well preserved. No nodules in optic nerve. *Second Eye.*—Tumour, similar type; shows great thickening of ganglion cell layer on approaching tumour.	...	One eye collapsed, being opened for diagnostic purposes.
Report by Mr. T. D. Marshall. Retina and vitreous full of small round gliomatous cells and neurogleial elements. O.N. appears healthy.	?	No recurrence. Child healthy, 1898, when last seen.
Report by Mr. Collins.	...	No recurrence. Child healthy, 1899.
L. globe (*Sagittal Section*). A.C. fairly deep. Pupil dilated. Post. synechiæ and angle blocked. Nerve appears thickened and in-filtrated. Vitreous shrunken. Retina de-tached. Large sub-retinal exudates con-taining hæmorrhage. Large tumour occupies whole of posterior half of globe. Contains large vessels with gelatinous-looking sheaths. Nerve involved. *Micro.*—Tumour a glioma; occupies posterior half of globe. Brown colour due to hæmorrh ges. Much necrosis. Vessels have sheaths of well stained cells. No rosettes. Reaches back of iris. Choroid extensively involved; optic N. involved. Has broken through especially at side of nerve. Dural nerve can be distinguished. Extra-ocular growth, less necrosis.	...	History. Child ran against perambulator, Nov. '04. Damaged L. eye. Gradual proptosis from this date. However, mother admits eye always looked glassy and different from other. *Under chloroform.* — Eye proptosed. In a central position, ¾ in. in front of cil. margin, somewhat dis-tended with engorged scleral vessels. No chemosis or pink zone. Corneal haze. A.C. shallow. Iris discoloured. Pupil dilated with green reflex. Large solid mass to be felt to inner side of orbit posterior to globe, and the whole of the contents at this posi-

SUMMARY OF CASES. Royal London

No. of case. Register No.	Name, surgeon, date.	Eye.	Age when growth first noted.	Age at operation.	Duration of life after operation.	Date of first sign of recurrence. Sites of recurrence.	Tension.
49 H.R.I. 654 O.P.	Alice Blummilt —*continued.*						
50 657 O.P.	♀ Mr. Parson's case March, '05	L.	...	...	...	...	...

Ophthalmic Hospital. 1897—1905.

Summary of Curator's Report.	Family history.	Remarks.
		tion were matted together. Growth appeared to be perforating sclerotic at posterior portion and surrounding optic N. R.E. apparently normal.
Sagittal Section. Cornea, A.C., iris normal. Lens *in situ*. Typical glioma exo. Choroid invaded in region of papilla. Free end of nerve seems uninvolved. Sclera seems intact. *Micro.*—Corneo-iridic angle blocked both sides. Iris cellular; cil. body normal. Retina totally detached; reaches close up to lens. Except for a short distance at ora serrata whole retina has undergone gliomatous degeneration. Tumour of usual type with much necrosis in anter. parts. True rosettes. Choroid involved in region of papilla. Scattered nodules also on surface. Pigment epithelium sometimes destroyed. Nerve head involved, and a few small nodules outside lam. cribrosa. Nerve at cut surface seems quite free. No evidence of extra-ocular growths.		

PAPILLOMA LIMBI CONJUNCTIVÆ.

By C. Pascheff, M.D. (Sofia, Bulgaria).

Primary papilloma of the conjunctival limbus, judging from the scarcity of recorded cases, seems to be very rare. During the six years of my ophthalmic practice in the Alexander Hospital in Sofia, I have observed four cases of this affection. In the present paper I shall record them shortly, and briefly review all the cases at present published.

Case 1.—A man, 56 years old, a farmer, in good health, had remarked for 15 days a small growth on his left eye. He had had no previous inflammation whatever in that eye.

Status Præsens.—The growth is situated on the nasal side of the limbus, and involves the conjunctiva more than the cornea. It is horizontally elongated like a pterygium, about 0·5 cm. in length, more prominent towards the cornea than towards the conjunctiva, and quite distinct from the latter, which is thickened and much injected around. It adheres to the cornea for about $1\frac{1}{2}$ mm., and has an extensive greyish edge. The growth, which in its middle attains a height of about 3 mm., is of a reddish-grey colour, with an irregular, strawberry-like surface. It is firmly attached to the cornea, and slightly movable with the conjunctiva over the sclerotic. The conjunctiva is normal elsewhere. The left preauricular gland is not enlarged.

The tumour was removed like a pterygium, and the edges of the wound sutured. As soon as the attachment of the tumour to the cornea was divided, the whole growth could be easily moved on the sclerotic. During the operation there was more hæmorrhage than in the excision of an ordinary pterygium.

Microscopical Examination.—The tumour was fixed and hardened in alcohol, and embedded in celloidin. The sections were stained with hæmatoxylin, hæmatoxylin-eosin, v. Gieson, picrocarmine, and Wiegert's elastic tissue stain.

The microscopical examination gives the following result:—(Figs. 1 and 3, Pl. VII, represent a section perpendicular to the

surface of the papilloma.) The fibrous layer of the conjunctiva near the growth, and especially under it, is much thickened and vascularised. The vessels are not only increased in number, but are greatly dilated, full of blood, and with thickened walls, especially the veins. Under them many elastic fibres closely pressed together are seen.

The adenoid layer is more distinct than normally; its fibres are loosened and separated by numerous small vessels and infiltrations of lymphocytes and mono- and poly-nuclear leucocytes. From this layer many connective tissue bundles with small thin blood vessels, consisting mostly of an endothelial wall, arise, and proceed upwards towards the epithelium. Some of these stems of connective tissue, before reaching the epithelium, divide like the branches of a tree into two or three other similar stems. All these branches and stems are covered with an extremely thickened stratified epithelium, thus constituting many *papillæ* of various sizes.

The epithelial cells which are in immediate contact with the connective tissue are cylindrical, short, and undergoing active proliferation. They rest upon a distinct thin membrane formed of a few fine, compressed, connective tissue fibres. Towards the periphery the epithelial cells become more polygonal and flatter. Some of them look swollen, are deprived of their nuclei, and stain very faintly. On the surface the cells are quite flat; some have lost their nuclei, but there is nowhere any actual cornification. These cells remind one very much of those which are met with in spring catarrh covering the nodular growths around the limbus.

The epithelium of the papillæ is almost everywhere much more developed than the connective tissue. The latter is infiltrated with numerous lymphocytes and leucocytes, some of which are even seen scattered in the epithelium of the papillæ. The epithelium, even where it is thickest, shows no cystic degeneration or epithelial pearls.

The corneal edge of the tumour (fig. 1) ends in a point, and shows clearly how the vascular connective tissue of the future papillæ invades the thickened, stratified epithelium covering it, and at some places begins to raise it. At the extreme edge the peripheral epithelium is somewhat swollen, and gradually passes

into the normal corneal epithelium. At the opposite edge of the tumour, towards the conjunctiva, the epithelium also passes into the normal conjunctival epithelium through a series of small undulations of varying thicknesses of epithelium, constituting what are called the "normal papillæ" of the conjunctival limbus.

Similar to this case are those published by Ayres (1), Norris (2), Sims (3), Goggin (4), and Grunert (5). In these the papilloma was much more developed, and was seated with a large base on the conjunctiva and cornea. In one instance it covered the whole of the latter (Ayres), and in another (Sims, Case 2) it stopped at the limbus, and instead of invading the cornea, overlapped it to the extent of $2\frac{1}{2}$ mm. The histological structure in all of them was more or less the same; once only a horny layer was observed covering the papillæ (Grunert, Case 3).

Some of the patients have suffered previously from conjunctivitis, and most of them were farmers. After the operation the growth has recurred in some instances. It was three times operated upon for recurrence in the case of Goggin.

Case 2.—A man, 30 years old, in good health, had noticed, 4 months before he was seen, a small growth on his left eye. It had increased very little since then. He had had no inflammation of the conjunctiva of that eye.

Status Præsens.—The little tumour is situated just at the centre of the limbus on its inner side, and with its long axis perpendicular to it. It is seated more on the conjunctiva than on the cornea, is horizontally elongated, and has distinct edges—overlapping both the cornea and the conjunctiva. It is firmly attached to the limbus by a short, slightly pedunculated base. Its length is about $4\frac{1}{2}$ mm., its greatest breadth 2 mm., and its surface is rough and of a rose-white colour. The conjunctiva around it is somewhat thickened, and with many blood vessels running towards the base of the tumour. Elsewhere it is normal. The whole growth is slightly movable with the conjunctiva over the sclerotic.

The tumour was easily detached from the limbus, leaving a bleeding spot which was touched with the galvanocautery.

Microscopical Examination.—(Fig. 2, Pl. VII, and Fig. 1, Pl. VIII, show a section perpendicular to the surface.) This growth is essentially a much thickened epithelial plaque, with distinct closely-set papillary formations in its base.

The epithelium is very regularly stratified, and covered on the surface by a thick layer of perfectly flat epithelial cells. The papillæ, although distinct and separate at the base, are almost uniformly united at the surface by the thickened, stratified epithelium. They are formed in the same way as in Case 1, and are infiltrated with many lymphocytes and leucocytes which invade their connective tissue and are seen also in their epithelial covering. The growth, having a broad, slightly pedunculated base, does not show so clearly as in Case 1 its true relations to the conjunctiva or the cornea.

On the surface of the tumour no distinct papillæ are seen, but rather undulations, except that near the cornea there is some indentation of the surface and a more truly papillary arrangement. Some of the superficial flat cells just in the middle of the section seem swollen, loosened, and even detached from the surface (Fig. 1, Pl. VIII).

A case published by Roche [6] was much more developed than this one, especially in height, and it had a more distinct peduncle. It was pyramidal in form, attached to the limbus by a short peduncle, and overlapped the cornea and still more the conjunctiva.

In the histological structure of the papillæ and in the relation between them this case resembles closely that described by Grunert (Case 3), in which the epithelial layer was thick and the papillæ so close together that one could not distinguish the exact limits between them. But it differed from the present instance in being covered on the surface by a horny layer.

Case 3.—A farmer, 55 years old, consulted me for a growth on the left cornea. It had begun 6 months previously like a

small grain on the inner margin of the cornea, and had been constantly growing towards the pupil.

Status Præsens.—The inner half and centre of the cornea are covered by a growth of a greyish-rose colour, and irregular mulberry like surface. It has the form of an isoceles triangle with the point covering the inner half of the pupillary area, and with the base directed towards the limbus. The base is a little concave towards the latter so that it touches it with its extreme points only, leaving thus a very narrow, slightly bi-convex space, within which the corneal surface has a greyish appearance and is markedly dull. The tumour is 6 mm. long, 3 mm. high, and 5 mm. wide at the base, where it arises almost perpendicularly above the conjunctiva. The latter all round the tumour is thickened, of a wine red colour, and deeply injected with numerous vessels which run towards the growth. The point of the tumour, occupying the pupillary area of the cornea, is also distinctly raised above the corneal surface, and is surrounded by a narrow band of thickened, greyish-coloured epithelium. The rest of the cornea and conjunctiva is normal.

The tumour was removed with the keratome from the surface of the cornea. There was considerable bleeding, especially towards the limbus. It was detached from the latter easily, and did not show any great adhesion to the conjunctiva. The corneal tissue on examination with the magnifier was sufficiently transparent, even near the affected limbus, to permit one to see a few deep centripetal blood vessels coming from the limbus and running in parallel lines in its substance. The wound was cauterised and healed completely in 3 weeks. The patient left the hospital with a superficial, fairly transparent opacity of the cornea in the former position of the growth.

Microscopical Examination.—The tumour was fixed in formol and hardened in alcohol; the sections were stained with hæmatoxylin, hæmatoxylin-eosin, picrocarmine and v. Gieson.

It is found to consist of numerous irregular papillæ of varying size, of which the epithelial elements are considerably more developed than the connective tissue (Fig. 2, Pl. VIII) represents a section of the advancing corneal edge of the tumour perpendicular to its surface. There is everywhere a distinct limiting membrane between the connective tissue and the basal

epithelial cells. The latter are cylindrical and longer than in the previous cases; they are set perpendicularly upon the membrane. On the surface the epithelial cells are quite flat, stain less than the others, but are provided with nuclei.

Bowman's membrane seems to be destroyed and absent especially towards the limbus. It is replaced by a fibrous tissue from which small stems with very thin-walled blood vessels arise, to form the axes of the papillæ. This connective tissue, rather poor in vessels, is infiltrated with many lymphocytes and leucocytes which are seen even among the epithelial cells. Fig. 2, which corresponds to the advancing edge of the tumour, shows cells similar in form to those of the deepest layer of the corneal epithelium—cylindrical, elongated and closely set. They stand upon the membrane, which can be traced underneath the neighbouring papilla and also upwards into its axis.

Case 4.—A woman, 50 years old, in good health, and without any history of previous inflammation of the eyes, had remarked 3 years previously a small growth on the temporal side of her right cornea. Since then it had grown constantly, and had covered the pupil, depriving her of sight in that eye. It was not painful and she had tried several times to get rid of it by tearing it off with her finger nails. Lately it had grown so much that she could no longer close the eye.

Status Præsens.—The growth covers almost the whole of the cornea with the exception of a small part of its supero-internal quadrant. It is of a rose-grey colour; its surface is cauliflower-like and it bleeds very easily. By its base it adheres very firmly to the cornea, and it is limited everywhere by the limbus, which is overlapped by its flattened peripheral edge. At its centre it is very much elevated above the corneal surface—about $1\frac{1}{2}$ cm.; so that it pushes forward the upper lid and has very much the aspect of a sessile mushroom. It seems to be made up of four lobes closely pressed upon one another. The conjunctiva around the tumour is somewhat thickened, vascularised and with much enlarged veins all running towards the base of the tumour. There was good perception of light.

The growth was removed and the surface cauterised. The patient left the hospital with vision = 4/50.

Microscopical Examination.—The growth consists of a number

of long thick well developed papillæ, with large vessels full of blood and very little connective tissue. The epithelium of the papillæ is very thick and stratified; its basal cells are in active proliferation, while the superficial are, in most of the papillæ, swollen and with badly stained or altogether absent nuclei [7].

This case resembles very much that given in the excellent work of Lagrange on the tumours of the eye (Vol. I, Pl. VI, Figs. 3 and 4), and for this reason I have abstained from illustrating it.

Along with these two cases may be reckoned all those which have begun either directly in connection with the limbus or merely in contact with it. These have been described by most authors as "papilloma of the cornea." Such are the cases of Professor Gayet [8], Lagrange [9], Démichéri [10], and Magnus [11]. Even the case of Dean [12] may be classified here, since the history which the patient gives in regard to the relation of the tumour to the limbus is of no decisive importance. Further even where there is some corneal epithelium separating the tumour from the limbus, it always presents changes which cannot be seen with the naked eye (Case 3).

From the study of all these cases we may make the following deductions with regard to the clinical, anatomico-pathological and etiological features of this peculiar and rare affection of the limbus.

Clinically the papilloma has more or less of a mulberry-like surface, which may become cauliflower like, especially on the cornea (Case 4). It develops rather quickly—from some weeks to several months—and very frequently recurs after operation. It is generally superficial and benignant, although it is said that it may degenerate into an epithelioma (Lagrange). Its colour is pale rose or reddish grey, approaching the colour of the fully formed palpebral papilla of spring catarrh. It appears at all ages; the youngest patient observed was 12 years old, and the oldest 71. It has usually been met with on one eye, and has only once appeared on both (Magnus).

As to its situation three types of *primary papilloma of the limbus* may be distinguished.

To the first type belong all those cases in which the papilloma begins on the conjunctiva and spreads towards the limbus and cornea. It begins anywhere on the conjunctiva around the limbus, and generally within a zone not wider than 4—5 mm. from it. It is always sharply limited towards the conjunctiva, and its peculiar feature is its advance towards the limbus and cornea, which it may entirely cover. Sometimes, however, it stops at its margin and if it still continues to grow, it overlaps it but does not invade it.

To the second type belong those cases which spring from the limbus itself, but instead of invading the cornea become pedunculated and grow in height rather than superficially. Some of these cases take on a pyramidal form and overlap with a large base both the cornea and the conjunctiva.

Under the third type is included the papilloma which begins at the limbus and develops entirely on the cornea. Here the epithelial part of the papilla is furnished by the cornea, but the vasculo-connective tissue comes entirely from the conjunctiva. The growth may cover the entire cornea but is always sharply delimited by the limbus, and has never been seen to invade the conjunctiva proper.

Histologically, the papillæ are of different degrees of development, single or ramified, but always of the same structure. In all the epithelial element is the predominant one, and is furnished by the conjunctiva or cornea according to the anatomical situation of the papilloma. Sometimes it is so hypertrophied that the papillæ are pressed together and on the surface of the papilloma one cannot distinguish the exact limits between them. In almost all cases the superficial cells are flat but not really cornified.

The connective tissue seems to be more abundant in the first and second types than in the third. In the latter it may be represented by a few fibres only which sustain the large well-developed blood vessels (Case 4). But in all these types the connective tissue is the same, coming mostly from

the adenoid layer of the conjunctiva. At the beginning of the corneal invasion it seems to advance between the epithelium which is already thickened and stratified and Bowman's membrane. Later, however, the latter is generally destroyed, but the cornea is never infiltrated by the epithelium, and clears up after the removal of the growth (Case 4).

In most instances the papillæ are infiltrated more or less with lympho- and leuco-cytes, which seem to furnish evidence of a previous inflammation.

As to the *etiology* of papilloma of the limbus, little can be said, except that in many cases a previous irritation or inflammation of the conjunctiva has been observed. In favour of this as a cause, the lymphoid infiltration of the papillæ may also be mentioned, and the fact that papillomata are usually met with in farmers and people exposed to ocular irritation. This, however, does not prove that they are always of an inflammatory nature.

The papillæ which are found normally on the conjunctiva near the limbus have generally nothing to do with the pathogeny of papilloma, for the latter may appear anywhere on the conjunctiva, as well as on other parts of the body where there are no papillæ [13, 14].

The interpretation which Goggin gives of his case, namely, that it was a simple hypertrophy of the epidermis and papillary layers of the conjunctiva, seems to me unsatisfactory, since his case is just the one in which the papilloma recurred the most frequently.

Of the four cases which I have reported here, perhaps the first seems the most closely connected with previous conjunctival inflammation, since it showed the greatest infiltration with lymphocytes, and the relation between the normal conjunctival epithelium and that of the papilloma seemed to be that of a *gradual* thickening and stratification.

In all other cases the papilloma remains a *special and definite tumour*, which may be influenced in its appearance by an exterior influence, but cannot be caused by it unless there is a special predisposition of the tissues to it. This

explains also its rarety, not only at the limbus, but also elsewhere on the conjunctiva.

In conclusion, I have to thank Mr. Coats for the photographs of my sections with which this article is illustrated.

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Description of Plates VII and VIII.

Plate VII.

Fig. 1, × 10.—General view of the papilloma from Case 1. The corneal edge is to the right.

Fig. 2, × 10.—General view of the papilloma from Case 2. The corneal edge is to the right.

FIG. 3, × 100.—High power view of one of the papillæ from Case 1. It consists of a central branching stem of vascular connective tissue, moderately infiltrated with lymphocytes and leucocytes. These are also found among the epithelium, especially in its deeper layers. The epithelium is greatly thickened, and its cells become flattened towards the surface and frequently lose their nuclei. There is, however, no true cornification.

PLATE VIII.

FIG. 1, × 100.—High power view of the tumour in Case 2. The connective tissue stems are small, single, and do not branch. The spaces between them are entirely filled in with epithelium, so that the surface of the tumour is not papillated, but smooth. The amount of epithelium greatly exceeds the amount of connective tissue. Some of the superficial cells are swollen and detached, but the nuclei are well stained quite up to the surface; there is no cornification. Both the epithelium and the connective tissue are infiltrated with lymphocytes and leucocytes.

FIG. 2, × 100.—Section of the central edge of the tumour in Case 3. The epithelium greatly preponderates over the connective tissue. Both are slightly infiltrated with lymphocytes and leucocytes. The thin line below represents a part of Bowman's membrane; a few fibres from this could be traced in some of the sections running up into the connective tissue of the papillæ to form a basement membrane for the epithelium, but this is not shown in the present section.

FIG. 1.

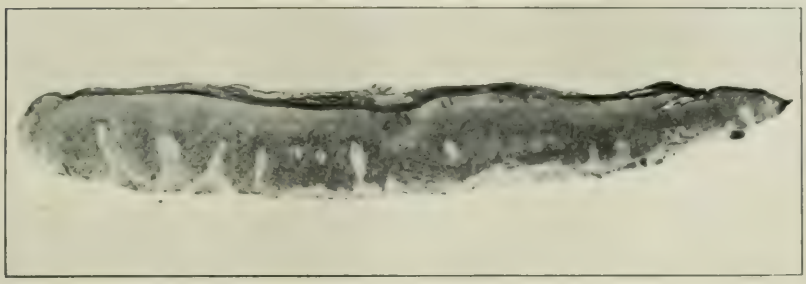

FIG. 2.

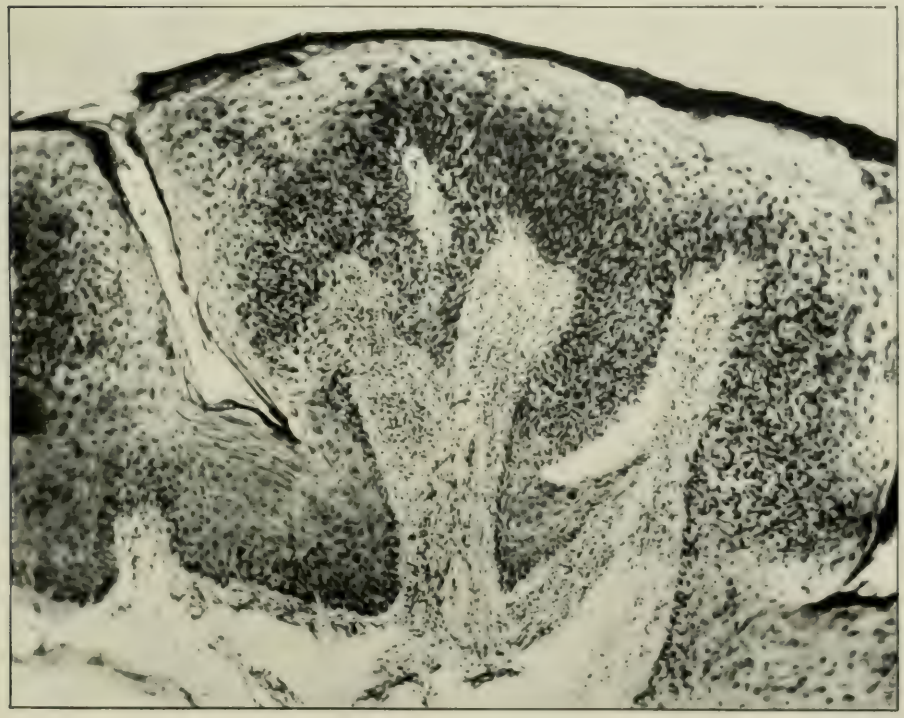

FIG. 3.

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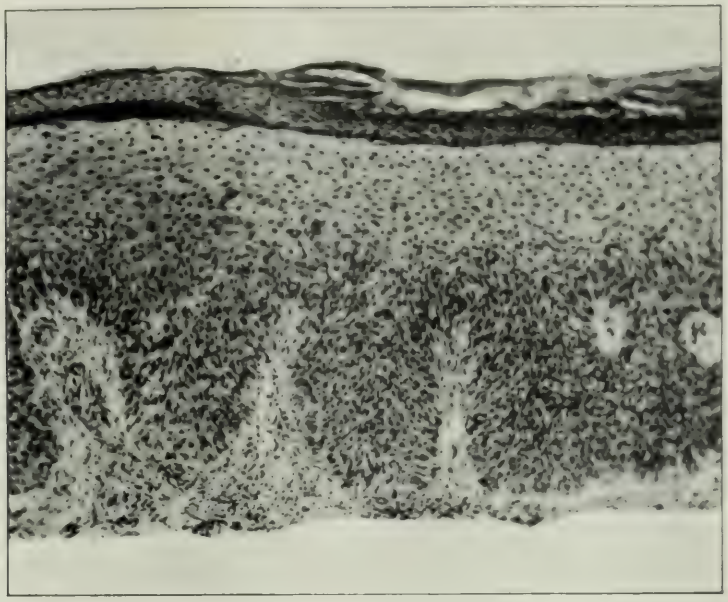

Fig. 1.

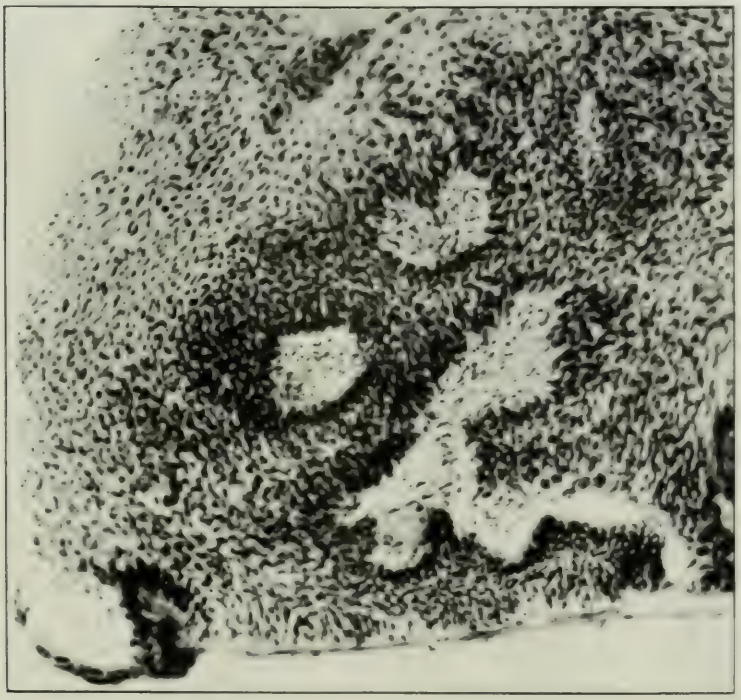

Fig. 2.

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A CASE OF TUBERCLE OF THE NERVE HEAD.

By George Coats (Curator),

Harold J., æt. 1 year and 4 months, attended the out-patient department of the R.L.O. Hospital on January 21st, 1905, under the care of Mr. Fisher. The left eye was said to have squinted and to have become "dimmer" during the previous three weeks. The cornea was dull; there was slight pericorneal congestion; the pupil was large and eccentric, and there were posterior synechiæ downwards and inwards. The tension was thought to be somewhat full, but the eyeball was tender, and the baby cried when pressure was exercised upon it. No view of the fundus could be obtained. In-patient treatment was at first refused by the parents, but a week later the child was admitted. He was, however, found to be very ill, with rapid breathing and a temperature of 102° F. Arrangements were therefore made for his transference to Great Ormond Street Hospital, where he was admitted under the care of Dr. Voelcker, to whom I am indebted for the use of the following notes.

The child had measles 10 weeks ago, and has been ill ever since. He has never been free from cough; there has been wasting, and the motions have been offensive. During three weeks he has been restless, and for the past fortnight he has been putting his hand to his ear as if in pain. The child was breast-fed until three weeks ago.

He is the last of 8 children; the first 4 were still-born, and there has been one miscarriage; the 7th died at the age of $3\frac{1}{2}$ years from empyema. The mother's father died of phthisis.

On admission there was right facial palsy. The right side of the chest showed impaired movement, and the apex was dull to percussion back and front. In the same situation there was tubular breathing, and there were crepitations in the lower part of the right lung. On January 30th he had a convulsion: both sides of the face twitched, especially the upper parts; the arms

and legs were flaccid; the eyes were turned to the right, and then there were movements of the head to the right; there was no incontinence. Later there were two other fits, and the child died on January 31st.

Post-mortem Notes (30 hours after death).—The lungs showed every stage of tuberculous invasion from miliary tubercles up to large walled cavities containing partially evacuated pus. There was tubercle of the larynx and of the bronchi, but without perforation. The intrathoracic glands were caseous and softened, equally on the two sides. Abdomen.—Tubercles in the liver, spleen, and kidneys. In the intestines, ulcers and miliary tubercles. Caseous mesenteric glands. Head.—There was a caseous patch at the left occipital pole on its ventral surface, and spreading upwards from this over the cortex and into the fissure of Sylvius; the dura was adherent to it, but there was no general tuberculous meningitis, as the right side was normal. Pus in the middle ear. The left eye was removed for examination; the right was not kept.

Pathological Examination of the Left Eye.

The globe was hardened in formol, frozen, bisected sagittally, one half embedded in celloidin, and cut in serial section.

Macroscopic Examination.—The anterior chamber is fairly deep. The corneo-iridic angle is blocked above; below it seems to be free, and on this side there is an adhesion of the iris to the lens capsule. The lens is *in situ*, and the vitreous clear. The retina is detached from the papilla to the ora serrata by a milky exudate. The optic nerve head is occupied by a yellow mass situated partly inside, partly outside the lamina cribrosa (Pl. V, Fig. 3). The intraocular part is quadrangular in shape, and measures 4·5 mm. in breadth by 3·5 mm. in height; the retina comes off from its anterior angles. Posteriorly, it overlaps the choroid for some distance without being adherent to it. The extraocular part is connected with the foregoing by a narrow neck, in the situation of the porus opticus. It measures 4·5 mm. longitudinally and 3 mm. transversely, and ends above with a well-defined rounded border. The nerve sheaths are distended where it is situated, and there are no isolated nodules. Around the nerve entrance

the choroid is only slightly thickened, and for a very short distance, and in no part of the uvea are there any visible nodules.

Microscopic Examination.—The cornea is normal. The corneo-iridic angle is blocked on both sides; above, the adhesion reaches as far forward as the membrane of Descemet, and the iris forms an acute angle with the cornea; its root is somewhat atrophic, its stroma cellular; there is ectropium uveæ; posterior synechiæ are not present. Below, the adhesion does not reach so far forward. The angle is rounded and filled in with new-formed connective tissue; the pupillary border is adherent to the lens capsule by connective tissue, and there has been some dragging at the corneo-iridic angle. The iris on this side is also infiltrated. There is therefore evidence of a plastic iritis, but there is no evidence histologically that it was of tuberculous origin—there are no giant cell systems or epithelioid cells. The retina is detached and much folded; its nuclear layers are well preserved, but there is a good deal of œdema of the inner layers. The rods and cones are very imperfectly preserved. The retinal vessels are full of blood; their walls stain very badly, and seem to be necrotic even far out into the periphery of the retina. In the subretinal exudate there are many groups of cells; they have large, pale, swollen bodies and small nuclei, and sometimes they contain a few spicules of pigment. They are probably swollen hexagonal pigment cells and leucocytes. Similar groups of cells are found in the anterior part of the vitreous. The lens and ciliary body are normal.

The mass in the nerve head (Pl. IX, Fig. 1) is a granuloma. There are no perfectly typical tubercle systems in it, but there are a few giant cells of the Langhans type. For the most part it consists of round and spindle-shaped cells. Blood vessels are very scanty, and where they occur show much narrowing of their lumina from endothelial proliferation and thickening of their walls. There is a good deal of caseation in the extraocular part, while the intraocular part is entirely necrotic except that it is lined at the sides by a thin layer of degenerated retinal tissue which retains its nuclear staining. Immediately above the mass the central vessels are normal; in the necrotic intraocular portion the vessels are also necrotic, and, as mentioned, they remain so for a long way out into the periphery. Where it passes through

the porus opticus the mass is much constricted, and the lamina cribrosa has been destroyed. The pia-arachnoid is slightly infiltrated, and there are a few small nodules on the inner surface of the dura near the globe; but the sheaths are mostly normal, the tissue has not been growing freely up the vaginal space. The nerve above the main mass is a little infiltrated and atrophic, but there are no isolated nodules in it.

The choroid is only involved for a very short distance round the nerve head—not more than a papilla diameter. It has evidently been secondarily invaded from the mass in the nerve. There is, on the whole, less caseation in the choroidal portion, and a few tolerably well-formed tubercle systems are found in it (Pl. IX, Fig. 2). A little distance from the papilla the infiltration ceases, and the rest of the choroid is empty of blood and condensed, but apparently normal. Tubercle bacilli were found in the mass in the nerve, but very scantily. Inoculation experiments could not be carried out, as the eye had already been hardened before the nodule was discovered.

The case belongs to a decidedly rare but fairly well-defined group—conglomerate tubercle of the nerve head. The histological characters of the mass itself were not absolutely characteristic, and might have supported a diagnosis of gumma, especially in view of the marked sclerosis of the vessels; and the finding of a very few giant cells would not have invalidated this diagnosis. But the discovery of tubercle systems in the better preserved tissues of the choroid immediately adjacent to the nerve, the finding of tubercle bacilli, and the clinical and *post-mortem* aspects of the case all place the diagnosis beyond dispute.

It differs from most of those on record in that the mass in the nerve head was the only one in the eye. Most other cases have had other nodules either in the retina or somewhere in the uvea. Iritis was indeed present, but it was an ordinary plastic iritis with no specific characters. It was apparently produced by tubercular toxines originating in the mass behind, and the case therefore raises interesting questions as to whether a simple iritis might be produced by

similar toxines circulating in the blood, without any other local lesion in the eye; that is whether in a tuberculous subject an iritis might be set up without any local settlement of tubercle bacilli. The supposition has been both asserted (Bürstenbinder) and denied. It has been maintained that in these cases nodules are always present, but so small as to escape clinical observation. In the present instance, however, the eye was examined in serial section, and they were quite absent.

The case in the literature which most nearly resembles the present one is that of Arnold Knapp. In a child aged 2, a white reflex had been noted from the pupil of the left eye which was divergent. The media were clear, the tension was normal, and there was no iritis. The retina was totally detached, and its vessels were visible on focal illumination. The eye was excised on suspicion of glioma. In the nerve head a mass was found extending back into the nerve with a sharply defined outline, and consisting of typical tuberculous tissue. Its intraocular portion was bounded laterally by the retina, which came off from its anterior angles, and was detached up to the ora serrata. There were two nodules in the choroid more anteriorly. Tubercle bacilli were found. No other evidence of tuberculosis was discovered at the time of operation, but a year later there was tuberculous disease of both elbow joints, cough, and hectic fever; there was no meningitis.

Spalding has also reported a case. A boy, aged 8, had symptoms resembling those of meningitis—rigors, headache, vomiting, retraction of the head, and apathy. Ten days later a yellow reflex was noticed from the left pupil; there were swelling of the upper lid, deep congestion of the globe, posterior synechiæ, discoloration of the iris, and ophthalmoscopically a yellow tumour in the vitreous, over which the retinal vessels could be seen to course. Enucleation of the eye was followed by relief of all the symptoms. The vitreous was one-third filled with a firm yellowish tumour arising from the optic papilla, more from its circumference

than its centre. Microscopically it consisted of necrotic tissue, small cell infiltration and giant cells. There was a funnel-shaped detachment of the retina. Tubercle bacilli were found.

A case of O'Sullivan and Story also closely resembles the present one, except that there was extensive involvement of the retina. A woman, aged 21, was seen 3 months after loss of vision in the right eye. There was a large white swelling in the region of the disc, with white spots about the macula. The eye was enucleated 3 months later. There was a mass around the nerve entrance 1/3 inch broad by 1/5 inch high, much like the one described above, according to the picture. It consisted of typical tuberculous tissue with caseation, and there were similar tuberculous nodules in the retina, which was detached. The patient was well 18 months later, except that she had been losing flesh and had pains in the back of the head. No tuberculous lesion could be discovered, however. Apparently the retina may be involved without the nerve, as in a case published by Hancock in the last number of these Reports, where also other similar instances are mentioned.

A case reported by Weiss belongs to the same category, but there was extensive tuberculous disease elsewhere in the eye. A man, aged 51, developed pain and lachrymation in the left eye shortly after an attack of pneumonia. There was peripheral corneal ulceration and iritis, with subsequent development of nodules. Later the sclera became staphylomatous, and the eye was enucleated $2\frac{1}{2}$ months from the onset of symptoms. In the nerve head there was a mass 6 mm. broad by 2 to 3 mm. high. It contained typical tubercles with giant cells, and these were also found in the course of the nerve through the scleral canal, but not outside. There were some nodules in the retina peripherally, and in the iris and ciliary body. The choroid was generally infiltrated, but showed no tubercles. There was no evidence of general tuberculosis.

Brailey's case is probably of the same kind. A boy, aged 2, had some degree of buphthalmos, a deep anterior

chamber, posterior synechiæ, and what appeared to be a detached retina. The tension was raised. Projecting from the region of the papilla there was a mass the size of a large pea, which pushed back the lamina but did not extend beyond it. It contained typical tubercle systems. The choroid in the immediate vicinity was much thickened by similar tissue which tapered off rapidly into unaffected choroid. There were a few patches in the adjacent sclera. Brailey inclines to think, on the ground of general experience, that the original focus was in the choroid, but points out that the main mass was in the nerve, and that the choroid was only involved in its immediate vicinity.

Less typical are two cases of Michel's. In one the retina was extensively involved, and there were also tubercles in the nerve head. In the other there were two isolated tuberculous nodules in the region of the lamina. In a case of Sattler's also the main focus was outside the lamina, but the intraocular portion of the nerve was also involved, and there were miliary nodules in the retina. There was extensive tuberculous disease of the orbit, and the child died 5 months later of tuberculous meningitis. A nodule was found *post-mortem* in the chiasma, and there were tuberculous bronchial glands. Kabsch has also reported a case with tubercles in the region of the lamina. A case of Emanuel's presents a superficial resemblance to the others, but has evidently originated in the choroid.

These are all the cases which I have been able to find in the literature, so that the condition is evidently a rare one.

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Description of Plate V, Fig. 3, and Plate IX.

Plate V.

Fig. 3.—Macroscopic view of the eye to show the mass in the nerve head and the detachment of the retina by a milky exudate.

Plate IX.

Fig. 1, × 9.—The mass in the nerve head. The intra- and extra-ocular portions are connected through the scleral canal by a narrow neck, and in this situation the lamina cribrosa has disappeared. The intraocular part is quadrangular, and is entirely necrotic except for a narrow rim of degenerated retinal tissue laterally. The retina comes off from the anterior angles and is detached. The extraocular part ends in a well-defined wavy line; it is much less caseous than the intraocular portion. The sheaths of the nerve are very little infiltrated, and show no tuberculous nodules. The choroid is only slightly involved, and for a very short distance around the nerve entrance.

Fig. 2, × 200.—A tubercle system in the choroid close to the nerve entrance. It shows round-cell infiltration, epithelioid cells, a giant cell of the Langhans type, and slight caseation near it.

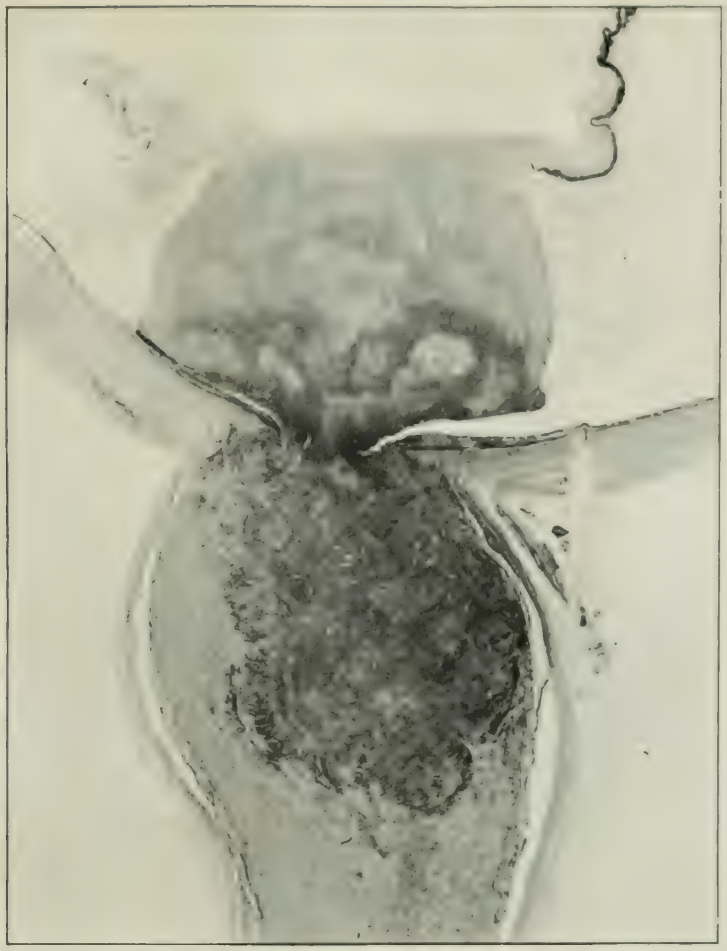

FIG. 1.

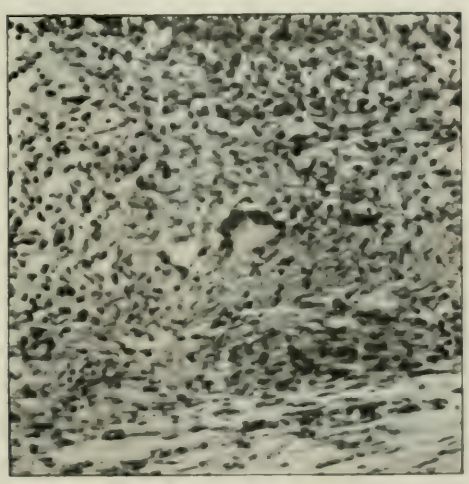

FIG. 2.

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ADDITIONAL CASES OF HEREDITARY CATARACT.

By E. NETTLESHIP.

SINCE the publication of a paper on hereditary cataract in the last number of these Reports, the particulars of several new cases have been sent to me by friends, and I have found the following published ones previously overlooked.

The classification of the cases is as nearly as possible the same as before, and the same signs are employed in the diagrams, viz.:—

♂, *Male.* ♂, *Male affected.*

♀ or ○ *Female.* ● or ●, *Female affected.*

○ or ●, *Sex not stated.*

◯, *Several siblings, i.e. brothers and sisters, unaffected;* if all are of same sex, the sex sign is added. A number within the circle indicates how many.

Parents joined by a bracket above, ♂ ♀, are cousins.

Twins are joined by a horizontal line above, ♂—♀.

A wavy line (~~~) *beneath a childship* means that the order of birth is not known.

Successive generations are indicated by Roman numerals (I, II, &c.), at the side of the diagram.

The numbering of the cases and diagrams is continued from the last (Case 97, Fig. 45) of the previous series. The reference numbers are also continued from No. 52 of the last paper.

Class A. ACQUIRED OR POST-NATAL CATARACT.

I. *Senile.* Case 98 (Fig. 46).—I regret that in my previous paper I omitted one of the most extensive recorded genealogies of hereditary cataract, that published

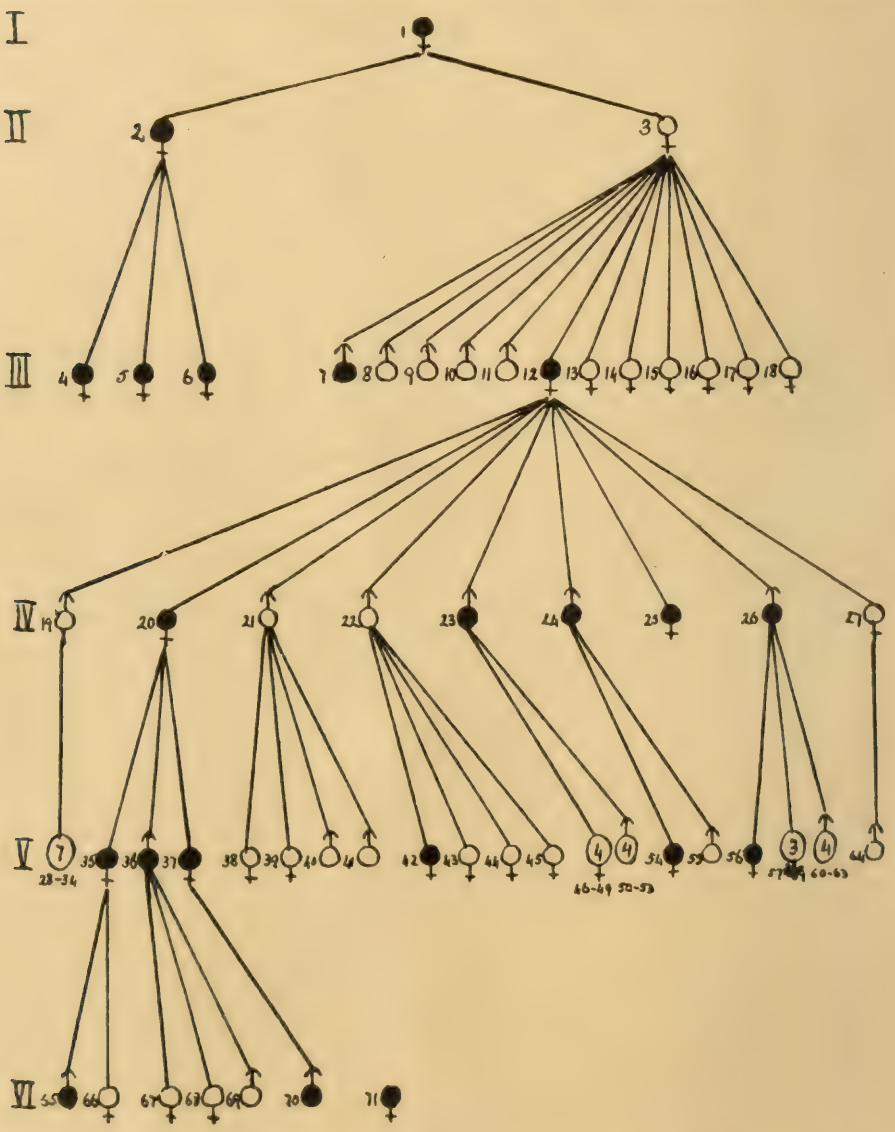

Fig. 46.

by Dr. John Green of St. Louis in 1890.[53] The pedigree is remarkable not only for its extent and the care with which it was worked out but for the strong evidence of "anticipation" (onset at an earlier age in each succeeding generation)

that it affords. I have kept the author's numbers for the various individuals.

Generation I.—(1) A woman who had cataract late in life. She had two daughters (*Generation II*, 2 and 3), of whom one (No. 2) also had cataract late in life. No. 3 appears to have been free.

Generation III, 4 to 6, three daughters of II, 2; all became cataractous late in life. 7 to 18, twelve children (five sons, seven daughters) of II, 3; the first-born (a son) had cataract late in life, the sixth (a daughter) showed signs of it at about 76, and when examined by Dr. Green in 1888 at the age of 83 had cataract complete in one eye, immature in the other. The other 10 children of II, 3, appear to have escaped.

In Generations IV, V, and VI, only the descendants of III, 12, were traced. III, 12, had nine children (IV, 19 to 27) of whom five (three male, two female) were affected, the cataract coming on between the 40th and 55th years of age. III, No. 12, and IV, 20 and 25, underwent extraction with good result.

In Generation V, containing 37 persons, there were six cases of cataract, and the disease is said to have appeared in all of them between 20 and 30 years of age. No. 37 was needled, but a well-defined nucleus coming forward into the a.c. within a few hours, linear extraction was performed (præsenile hard cataract); result excellent.

Generation VI seems to have consisted of only seven persons at the date of publication; three of the seven are known to have become affected between the ages of 6 and 9; all were treated by needling and solution, and obtained good vision. No. 35 (Generation V) was also treated by simple discission and did well, without evacuation of the lens. The exact parentage of VI, 71, was not noted, but she was the daughter of one of the females in Generation V, and her mother was said to have had perfect sight.

Of the 64 persons whose sex is stated 27 were males with 8 cases of cataract, 37 females with 14 cases, a relative excess of affected females over affected males in the proportion of 38 per cent. to 30 per cent. It will be noticed that though the descent was usually continuous, it was broken by an unaffected mother, No. 3 in Generation II, and by an unaffected father,

No. 22 in Generation IV; that in the offspring of these two, the proportion of affected to unaffected was small; and that of the 10 parents who transmitted the cataractous tendency, 7 were female, 3 male. As, however, the descendants of only one member of Generation III could be traced, the above figures are not conclusive.

CASE 99.—Senile cataract, anticipating and becoming præsenile; four generations involved. Additional case, communicated by Mr. J. Herbert Fisher (May, 1906).

Thomas Hawkins had early senile cataract at the age of 48 (1900); he also had glycosuria. His (Thomas Hawkins's) son, seen at the same time, had opacities in his R. lens (seen by Mr. Fisher).

His (Thomas Hawkins's) mother was operated for cataract at Oxford, and her father was also operated for cataract.

II. *Præsenile and Juvenile Cataract.*

Mr. E. C. Green, of Derby, sends me the following case.

CASE 100.—Father and mother healthy, with good eyes; issue six, of whom three have had præsenile cataract.

1. ♀ æt. 39 (1905), no cataract, but has been insane for a time.
2. ● Developed cataract rapidly at the age of 33; operated.
3. ● Cataract in one eye at 34, and six months later in the other; first eye operated, second eye not yet ready (1905).
4. ○ Died in infancy.
5. ○ Good eyes, married and has healthy children.
6. ● Cataract in both at 27, rapidly matured and operated.

The three girls with cataract were anæmic, prematurely aged, and intellectually dull, but none had grey hair. The opaque lenses were very white but not hard; all did well. No consanguinity of parents, and none known further back. Father was 12th of a childship of 15, married at 27 and died at 37; had good eyes. Mother was 3rd of 9, married at 26; still living, æt. 66, and sees well. None of the uncles, aunts or first cousins of the cataract patients have had cataract.

CASE 101.—Hall[54] in 1891 saw a man of 40, apparently a

native Indian, with complete cataract and "very opaque capsules," with evidence that the cataract had been present and progressing slowly for many years; one eye was operated with success. He brought three sons for examination, aged 18, 11, and 7, all showing "anterior polar cataracts in various stages of development."

Millikin[55] recorded the following in 1904.

Case 102, Fig. 47 (Author's Case 1).—Complete juvenile cataract in three generations. In Generation III, the first-born was a girl; cataract began in R. at æt. 9, and rapidly became complete; L. followed at æt. 13; both needled and did well.

Second, boy, cataract formed in both æt. 6; complete when seen at 8. One eye operated and did well. No other issue.

Generation II.—Mother operated successfully for cataract when a "girl." Her mother (Generation I) also operated successfully for cataract when "a young girl."

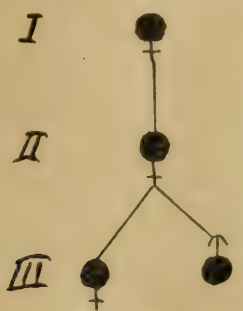

Fig. 47.

Schnabel[56] has published the following examples of heredity of cataract acquired in early childhood in two generations.

Case 103, Fig. 48 (Author's Case 3, Turi).—Father normal. Mother had double cataract removed by operation at the age of

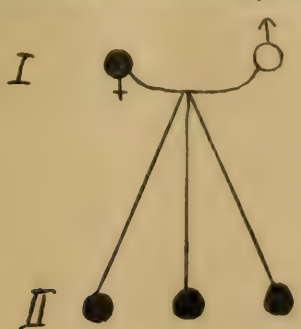

Fig. 48.

3 years with very good result; the cataract had appeared about six months before operation. Of her three children the eldest showed total soft cataract of L. eye at the age of $1\frac{1}{2}$ years and was examined at æt. 8; the second had total soft cataract of L. at æt. 2 and was examined when 5; the third had total soft cataract of both at æt. 1 year and was examined when 2.

Case 104.—In another case of Schnabel's (name not given) the father had been operated upon in childhood for cataract in both eyes with good result. Of his children (number not stated) two, who were born with normal eyes, developed cataract at 5 and 3 years old respectively.

Case 105 (Fig. 49).—Schnabel's third case of this form of hereditary cataract (Gärtner family) is as follows:—

Generation I.—A woman, herself with normal eyes, was one of a childship of 6, of whom 3 became blind from cataract in early childhood; the parents had good eyes. This woman married twice, both husbands having good eyes. By 1st husband, 2 normal children; by 2nd husband 5 children, of whom 3 were blinded by cataract in both eyes in early childhood. (Sexes and order of birth not given.)

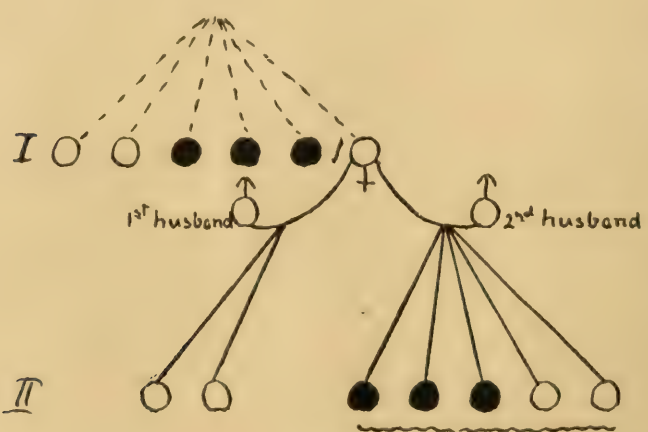

Fig. 49.

Case 106, Nolte[57].—Case of juvenile complete cataract in one generation only.

Family of Debus. Parents have good eyes; no consanguinity. First-born, Maria, had some convulsions during her 2nd year;

between 5 and 6 sight began to fail; admitted when aged 7 with general nearly complete cataracts and shallow a. cs. (= swollen lenses); operation, good result. Second, George, born about 1 year after No. 1; scarlet fever and "typhus" when æt. 6; sight quite good till æt. 6, when it failed. Seen æt. 8 with double cataract L. complete, R. chiefly posterior cortex. No fits. Third, Johannes, born 7 years after No. 2; sight good until æt. 6½; when seen 6 months later (æt. 7) double general cataract, chiefly of anterior and posterior cortex, not zonular. History of a feverish illness lasting about a week some months before V. began to fail, and of otorrhæa soon after.

All three children appeared in good health when seen.

CASE 107, from Mr. E. C. Green.—Father, an intelligent farmer, was operated upon for cataract in both eyes when æt. 9; he is now 48, and his eyes keep good. His four brothers and sisters all had good sight. No consanguinity between his parents nor between him and his wife. He has had only three children; all are living.

No. 1. ♂ Sight good till age of 5 years, when first R. then L. became cataractous, and were rapidly complete; needled. Robust and healthy.

2. ♂ Sight good till age of 5 years, when posterior polar cataracts began; became rapidly worse, and were needled. Robust and healthy.

3. ♀ Now (1906) æt. 6. Father reports her sight good.

B. CONGENITAL CATARACT.

I. *Lamellar Cataract.*

CASE 108 (Fig. 50).—Mr. Herbert Fisher allows me to use the following important case of hereditary lamellar cataract from his practice at Moorfields, and I have to thank Mr. Payan Dawnay for much help in investigating the history. I have seen the notes of all the cases, and have examined all the five affected, and some of the unaffected, children in the third generation. I believe this case to be the most extensive of its kind on record.

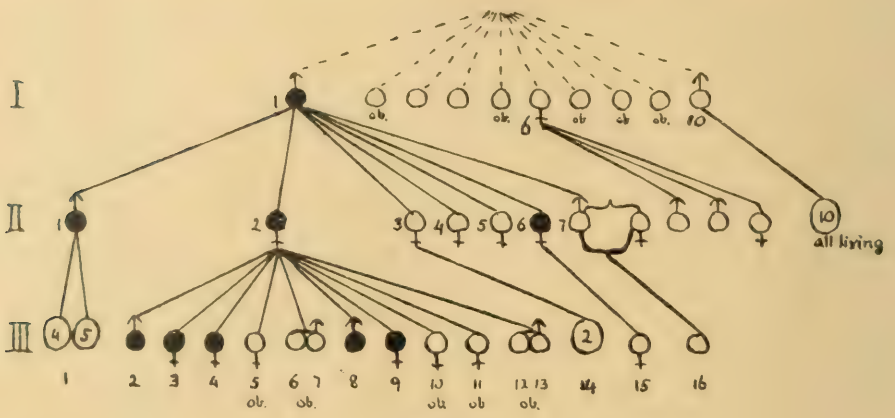

FIG. 50.

Generation I (1).—Charles Smith, now (1906) an old man, underwent discission by Mr. Bowman at Moorfields, first in one eye then in the other between the ages of 10 and 13 (1847, etc.). The entry in the Register on each occasion is "Congenital cataract." Many years afterwards a further needle operation was done by the late Mr. George Lawson for closed pupils and increased tension. He has now been totally blind for at least 15 years. He was the first-born of 10, of whom 5 died in early childhood and 5 (including himself) are living. All the living ones except No. 1 see well; the 6th (I, 6) is married and has 3 normal children, all living; the youngest, a Thames pilot (I, 10) has 10 children, all living and normal.

Generation II (1 to 7, children of I, 1).—No. 1, Charles T. Smith, told that he had cataract by the late Mr. George Lawson at æt. 18. Now æt. 40. Examined by Mr. Payan Dawnay April 28, 1906; dense lamellar cataract in each eye, the R. one showing a double shell of opacity; with R. reads 4/60, and 2 Jaeger at 8 inches.

No. 2, Emma, was operated for lamellar cataract at Moorfields in 1886 at the age of 18; she has recently had her loosened upper incisor teeth extracted; her lower incisors show imperfect enamel.

No. 6 (Florence) was also needled for lamellar cataract in 1886, when she was 9, and did well. Her first molar teeth were deficient in enamel. (Mr. Treacher Collins's note.)

I have examined No. 5, who was reported to have defective

sight, and found her lenses quite clear; eyes hypermetropic. The other 3 (II, 3, 4, 7) see well. No. 7 married a cousin, but has normal children.

Generation III has contained 24 persons. The first childship (III, 1) of 9 was the issue of II, 1, who has the cataract; the fifth was born dead; the first, second, third, and seventh died of measles, etc.; the fourth ♂ 11, sixth ♂ 8, eighth ♀ 7, and ninth ♀ 4 are living; I have recently examined them all, and found their lenses perfect. Only the eldest has permanent teeth, and they are normal. They are healthy, well grown children, and very intelligent.

The 2nd batch (Nos. 2 to 13) contains the children of II, 2, 10 births with 12 children (twins twice). Five are living, and I have seen them all; the first-born, William, third Emma, and seventh Edward, have been operated upon at Moorfields for lamellar cataract; whilst the second, Annie, æt. 14, and eighth, Lily, æt. 7, have typical lamellar cataracts and need operation (March, 1906). The fourth (III, 5) died at æt. 3 years; ninth (III, 10) died at 5 months, and was probably an idiot; the tenth (III, 11) died at 11 or 12 months. In each of the two twin-pregnancies, one miscarried at 4 months, the other (a boy in each instance) was born at full term; one of them dying at 5 months, the other at 12 months old. Thus every one of the 5 who were born alive and survived had lamellar cataract. In regard to the teeth of these 5 children, the permanent incisors are quite sound and well-shaped in all who have cut the permanent set (in the two youngest, III, 8 and 9, only the lower permanent incisors are up); the 1st permanent molars show deficiency of enamel in the two eldest (III, 2 and 3), but appear to me to be perfect in the other three (III, 4, 8, and 9). Some of the younger ones had convulsions. All the five living children are bright, intelligent, and well nourished, but the first and second-born are very undergrown.

In Generation I and the second-childship (2 to 13) of Generation III the infant mortality was very high; but, on the contrary, every member of Generation II has lived to adult age.

The other cataractous sister of II, 2 (viz., II, 6), has at present only one child (III, 15) believed to be normal. The normals II, 3 and 7, have normal children.

Case 109 (Fig. 51), Kunn [58], (1889), published, from Fuchs's practice, the following case of lamellar cataract in three generations.

Generation I, 1.—Cataract in early life, no details.

Generation II, 1.—Her daughter, operated by Arlt at æt. 6 for lamellar cataract and still sees well. Square ("rickety") skull.

Generation III, 1 to 4.—Issue of II, 1, order of birth not given. Two are normal; the other two, boys of 7 and 5 years (Nos. 1 and 2), had lamellar cataracts which in No. 2 was diagnosed at æt. $1\frac{1}{2}$ years, and showed a threefold layer of opacity; they had no fits, but their bones were rickety and they had "rachitic" teeth. (The youngest boy's teeth would still be the milk set.—E. N.)

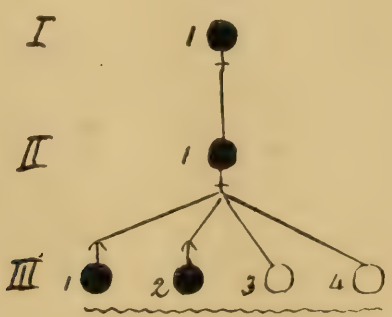

Fig. 51.

Case 110 (Fig. 52).—In 1893 Fromaget [59] published the following case of congenital, probably lamellar, cataract hereditary through five generations. Transmission was continuous throughout, and, except for the first generation, always took place through the mother. The cataract in the children (Generation V) consisted of "alternate opaque and clear layers"; two of the patients (III, 2 and V, 1) had had iridectomy performed in childhood. Probably, therefore, the cataract was lamellar in all the cases. In III, 2, at the date of publication the cataract seems to have been complete, but the patient declined further treatment. Her mother was the youngest of four daughters who had cataract from birth (Generation II); their father and one of his brothers were also reported to have had congenital cataract (Generation I). Of the four in Generation II, three had

gone out of reach and nothing more was known of them; only the mother of Generation III could be traced. III, 2 (Mde. P.), had 14 children, of whom two were born with cataract (IV, 1 and 2), a son and a daughter. The son was unmarried, the daughter (IV, 2) married, and at the time of writing was aged 28 and had had six children (V, 1 to 6); No. 1, aged 11, had undergone iridectomy for her cataracts at the age of 8; No. 4, aged 5; and No. 5, aged 3½, also had double congenital cataract; Nos. 2 and 3 were not affected; and No. 6, who died at the age of 3 weeks, was also believed to be free. No consanguinity of any of the parents.

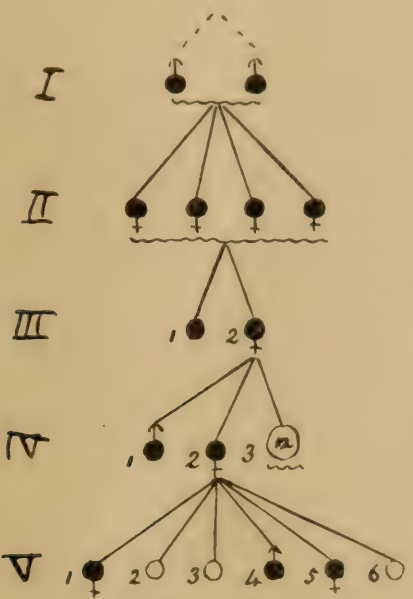

FIG. 52.

CASE 111 (Fig. 53).—Nolte's [57] case (Becker) is as follows:—

Generation I, 1.—Mrs. Becker, cataract formed in both eyes after whooping cough, at the age of 12 both were needled, L. lost by injury some years later. No. 2, her husband, good eyes. Issue, five children, viz.:

Generation II, I.—Christopher. Normal, has four normal children (III, 1).

2. Marie. Cataract, said to be lamellar, not examined.

3. Mathäus. "Lamellar" cataract diagnosed soon after birth. At about the age of 6 optical iridectomy down—in each

eye. When 18 (1879) patient badly developed, severe nystagmus, corneal diameter 10 mm., in each lens a central opacity with projections into the cortex and in R. the cortex is cloudy. R. needled now, and again in 1889. In 1895 R. with +10 D, fingers 3 m., some remains of lens. L. cortex now opaque in coloboma, V. Fingers $1\frac{1}{4}$ m., lens removed, good operative result V. +10 D, fingers 10 m.

4. Elise, normal, has one normal child.

5. Child (sex not stated) with lamellar cataract. Died in early infancy.

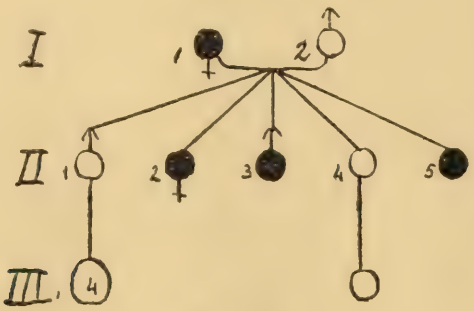

FIG. 53.

II. CASE 112 (Fig. 54), Zirm [60] and Bergmeister's case of *Congenital stellate cortical cataract* (*partly published, partly communicated by Professor Bergmeister*).

The particulars furnishing the following extensive and exhaustively worked out pedigree were published in part by Zirm, at that time First Assistant at Vienna, in Zehender's Klin-Monatsbl., January, 1892, pp. 5 to 30, and postscript, p. 40; and again, in ignorance of Zirm's paper and with the important addition of Generation VI, by Professor Bergmeister at one of the Vienna medical societies on December 3, 1892. *Case* 47 *in my former paper, erroneously attributed to Ziem, gives part of the same pedigree.* Professor Bergmeister informs me by letter that the whole family (name Löwy) was Jewish, but that as to consanguinity he has no information; nor is consanguinity mentioned by Zirm, in his otherwise full report. The first of the series to be seen was Eugen Löwy, No. 8 of Generation V, a boy of 14 whose case Zirm describes at length as a type of all the

others, illustrating it with two figures. Zirm says that a similar case described by Otto Becker from Arlt's clinic, years before, had since been ascertained to be one of these Löwys.

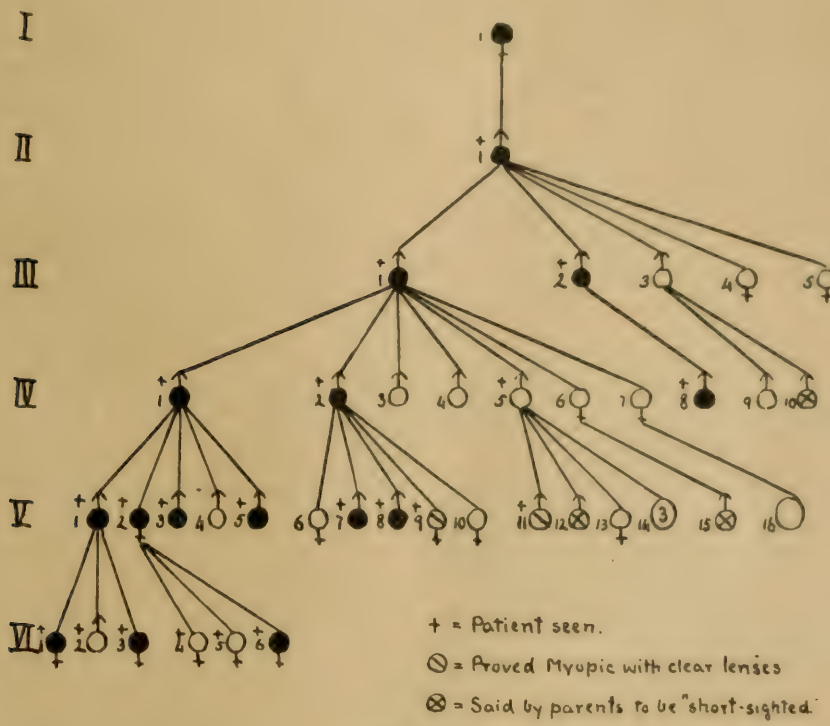

FIG. 54.

Generation I, 1.—Woman became blind, cause unknown.

Generation II.—Son of I, 1. Senile cataract. Had five children (III, 1 to 5). His wife had good eyes.

Generation III, 1.—Moriz L. Both eyes operated for senile cataract. His descendants are shown in Generation IV, 1 to 7, and Generations V and VI.

Generation III, 2.—Samuel L., when æt. 71 found to have stellate cataract. His only child (IV, 8) has the same form of cataract.

Generation III.—3, 4, and 5 all see well. No. 3 has two sons (IV, 9 and 10).

Generation IV.—1 to 7, issue of III, 1. 1, Samuel L., æt. 57 to 58 (1891 and 1892), mixed stellate and senile cataract both eyes, almost complete in L., in R. closely resembling the stellate cataract in V. 8 (below). Strong man with normal bones.

2. Max, 43 to 45, V. defective *from early life*, now stellate cataract with also numerous punctate opacities. My. 1/6 V. corrected = 20/70, fundus badly seen. Bones and teeth normal.

3. Alexander and 4 Adolf, both dead, no details. (The great difference of age between 1 and 2 suggests that Alexander and Adolf really came between Samuel and Max.—E. N.)

5. Leopold, 42. Lenses clear, fundi normal. Both Em., R. full V., L. 20/100 and 16 J. = congenital amblyopia without history of squint.

6 and 7. Daughters, good eyes, married.

8. Moriz, 40. Stellate cataract. No issue.

9 and 10. Sons. One has good eyes, the other said to be "short-sighted."

Generation V.—1 to 5 issue of IV, 1.

1. Jacques, 34 to 35. Stellate cataract, My. 4 D, V. corrected 20/50, unaided 2 J, held very close. Ophth. n. no posterior staphyloma. Teeth n. Health good.

2. Rosa. Stellate cataract. Married.

3. Max, 23. Stellate C.

4. Henri, 21. Normal eyes.

5. Lothar, 16. Stellate C.

Generation V.—6 to 10, issue of IV, 2.

6. Mathilde L. Good sight, "not short-sighted."

7. Isidor, 19 to 20. Stellate C. My. about 4 D. V, corrected 20/50 Ophth. n., no posterior staphyloma. Bones and teeth n.

8. Eugen, 14. Came for glasses in April, 1891; delicately built but healthy, teeth good, no signs of past rickets. *Sight somewhat defective as long as he can remember.* By focal light the anterior cortex of each lens shows five long radial striæ which become enlarged (club-shaped) at peripheral end; at posterior cortex a second stellate figure of three primary spokes dividing into six, all broader, shorter and somewhat denser than the anterior spokes; between the anterior striæ, especially the lower ones, delicate punctiform and linear spots. By transmitted light many finer striæ come into view. All of the opacities stop short of the equator, leaving that part quite clear. Fundi n.; V, My. 4 D, corrected 20/70. Appearances well shown in Zirm's Plate, Figs. 1 and 2.

9. Paula, 11 to 12. Lenses clear; My. R. 1/10, L. 1 18, no note of V.; Fundi n. No posterior staphyloma.

10. Sidonie, sees well, "not short-sighted."

11 to 16. Children of IV, 5, 6, and 7. Of these only No. 11 was examined; he had corneal nebulæ, no cataract, My. 4 D, without posterior staphyloma, V, corrected 20 50 partly with the better (R.) eye.

Nos. 12 and 15 said to be "short-sighted," all the others reported to have good sight.

Generation VI.—1 to 3, issue of V, 1. Seen and described by Bergmeister only.

1. Hilda, L. 8 (December, 1892). Stellate C.

2. Marcel, 5. Normal.

3. Erna, 4. Stellate C.

Generation VI.—4 to 6, issue of V, 2, seen by Bergmeister only.

4. Lina, 9, and 5, Marie, 7; both normal.

6. Friederiecke, 5. Stellate C.

Zirm mentions another isolated case of C. Stellata in a boy (like the Löwys, a Jew) in whom the refraction was H 5 D, and concludes therefrom that in those of the Löwy family who were both cataractous and myopic (*e.g.*, IV, 2, V, 1, 7 and 8 on pedigree) the My. was axial not lenticular. (He might also have cited Case V, 11, where there was My. with clear lenses.—E. N.)

III. *Other Varieties of Congenital Cataract.*

Case 113, Fig. 55. Millikin [55] (Author's Case 3.)—German family. Congenital cataract in two generations, combined with axial myopia.

Generation I, 1.—Mother æt. 44, examined and eyes found normal.

Generation I, 2.—Father æt. 46, both eyes operated for cataract about æt. 40; fundus showed myopic changes. Had all his life had poor sight, but no positive information whether cataracts were congenital.

Generation II, 1 to 7.—Issue of 1. Nos. 1, 2, and 7, good eyes; no note of their refraction.

Nos. 3, 4, 5, and 6, all showed "congenital central opacities of lens varying somewhat in shape and size" with V. from 3/60 to counting fingers. Eyes well formed and patients well grown. All 4 were operated upon with good results. Nos. 4 and 5 had H. only 6 D. and 7 D. respectively after operation, and must therefore have been myopic before.

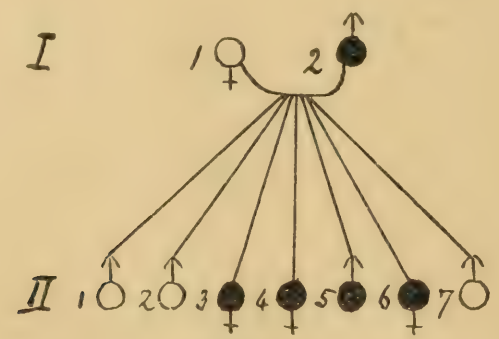

Fig. 55.

Case 114, Fig. 56. (Millikin gives the following, Case 2.)—Congenital cataract in 5 females, in three generations; lenses small and hard.

Generation I.—A Swedish woman operated for congenital cataract; age at operation not stated. *Generation II.* Her two daughters both operated for double congenital cataract, No. 2 when 6 years of age, No. 1 when young. No. 2 died 6 months after operation. No. 1 grew up and had two daughters (no other children); both were born with double cataract; (III, 1 and 2). III, 1, needled at æt. 9 months and did well; lenses small and hard. III, 2, not operated till æt. 5 years, but did well. All the five cataractous subjects were strong and healthy.

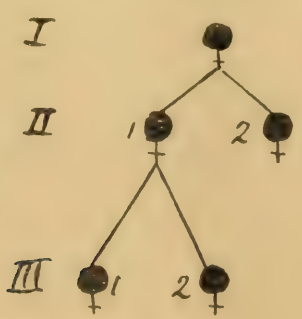

Fig. 56.

Schnabel [56] gives the following two cases of congenital "nuclear" cataract in several siblings, without evidence of inheritance from parents, grandparents, or any other relatives.

CASE 115 (Author's Case 1, Orthaber).—Three siblings aged 8, 6, and 3 years with double "nuclear" cataract.

CASE 116 (Author's Case 2, Lechner).—Three siblings aged 6½ years, 3 years and 8 weeks with double "nuclear" cataract.

CASE 117.—Guiot [61] Année Méd. de Caen, 1890, XV, 264.

A young mother with double congenital cataract which had been operated with poor result. Her first-born child (male) seen at three months of age with "incomplete central" cataract in both eyes.

CASE 118, Fig. 57.—Nolte [57] gives the following example of the occurrence of hereditary (doubtless congenital) cataract, and of other defects, including partial albinism without cataract, in various members of a family named Steitz.

Generation I, 1.—Mrs. Steitz (née Heppel) æt. 47, nuclear and general cataracts, both extracted with success; age at onset not given. Her brother (I, 2) was blind from cataract at æt. 43.

Generation II, 1 to 3.—Seven children of I, 1; of these 5 appear to be normal, but the first-born (1) Christine, 22, has "indications of hare-lip," though otherwise normal; and the 2nd, Maria, 18, has very fair complexion and fundus of eye highly deficient in pigment (the word albinism is not used either here or for the similar cases below, nor is there any note of V.; but Author intimates clearly that he considered the condition abnormal).

Generation II, 4 to 8.—Children of I, 2.

4. Katharina. Posterior polar and zonular cataracts in both eyes.

5. Elizabeth, 23. Congenital deficiency of pigment at fundus. No note of V.; II, 1 D.

6. Jacob, 18.
7. Heinrich, 12. } Both show the same deficiency of ocular pigment as Nos. 2 and 5 above. No note as to V.

8. Son, idiotic and with over-ripe cataracts.

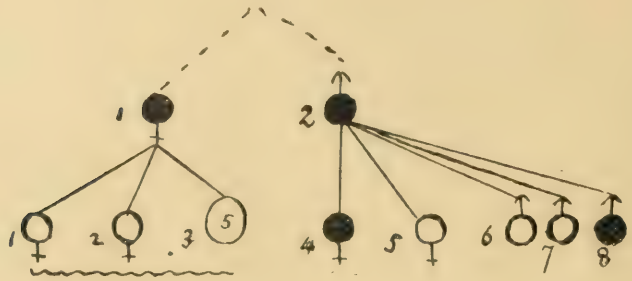

FIG. 57.

CASE 119, Fig. 58.—Pisenti [62]. Congenital shrunken cataract, nystagmus and hydrocephalus in 3 of 6 children. Parents first cousins, who themselves inherit mental degeneracy.

Generation I, 1.—Died insane.

Generation II, 1.—Paul, imbecile. Two brothers were epileptic; of his 5 sisters 2 were hysterical, 1 had religious mania, and 2 were tubercular. Paul married II. 2, not related by blood; she had 1 sister (Annie, II. 3), who married an "eccentric" man (3a), and after bearing three children (III. 5 to 7) died at æt. 30 probably of some disease of nervous system.

Generation III.—1 to 4 issue of II, 1 and 2. No. 1 died of tubercle æt. 18; 2 and 3 had religious mania; No. 4 married his maternal first cousin (III, 5), whose two brothers (6 and 7) had

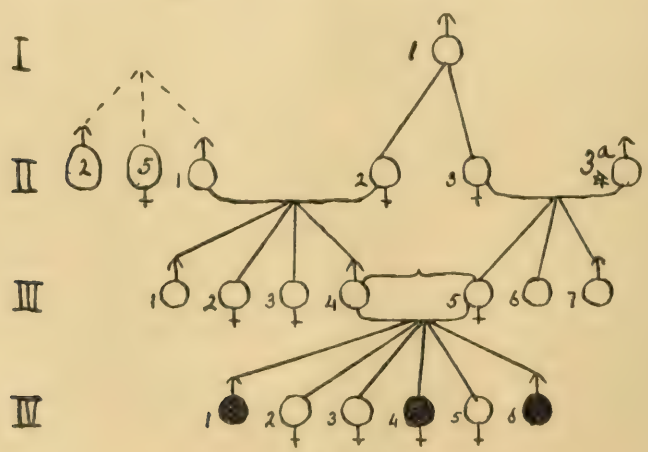

FIG. 58.

weak intellect and alcoholic mania respectively. The cousins, 4 and 5, are not stated to have been unsound, but their children (*Generation IV*, 1 *to* 6) were as follows:—

1. Dead.
4. Living, æt. 4½.
6. Milk teeth carious.

} These three had shrunken congenital cataract and nystagmus, with hydrocephalus.

2 and 3, living and fairly normal; 2 has convergent squint.
5. Died (æt. 3) of tubercular meningitis.

CASE 120.—Congenital cataract, probably complete, running through 4 generations and affecting 15 persons. A. D. Williams, 1880[63]. Order of birth not stated.

Generation I. ↕ Blind from congenital cataract. Had 4 blind children (Generation II), and some not blind (number not stated).

II, 1. ↕ Congenital cataract; had 7 children (Generation III), of whom 3 (III, 1, 2, 3) had the same cataract.

„ 2. ↕ The same kind of cataract; had 2 children (Generation III, 4, 5) similarly affected.

„ 3. ↕ Same cataract. Had 5 children (Generation III), of whom 1 (↕ III, 6) and 1 other (III, 7) (sex not stated) affected; 3 unaffected. The cataractous son, III, 6, had 4 children (Generation IV), of whom 3 (IV, 1, 2, 3) were blind from cataract, and inmates of the St. Louis Blind Asylum.

„ 4. ● Fourth cataractous child of I, 1; no particulars.

Postscript to Case 46 *of previous paper, p.* 209 (*Fukala's case*).

Reference to the original paper has since allowed of more precision as to the age of onset of the cataract in several of the patients. In No. 1 (*Generation I*) *it came on at* 40 *years of age, in Nos.* 2 *to* 10 (*Generation II*) *between* 20 *and* 40; *in the three patients indicated by No. II* (*Generation III*) *at* 20, 22, *and* 23 *respectively; and in the first of the three indicated by No.* 13 (*Generation III*), *a woman, the cataract was present at* 30. *The condition was, therefore, præsenile in probably all, with some, but not very marked, "anticipation."*

Postscript.—The proof of the above had been corrected before I saw the paper by Dr. Casey A. Wood on the same subject, giving three new cases (Ophth. Record, vol. xv, p. 142, April, 1906). The cases are :—

1. *Charlton.*—4 generations : I. ♀ blind from cataract. II. Daughter of I, free. III. Daughter of II, cataract. IV. 12 children of III, of whom 10 (5 ♂, 5 ♀) have juvenile cataract ; it is not clear that all these 10 were examined, but in one of them, ♀ æt 33, the cataract is lamellar ; Nos. 10 and 11 of this childship, free, both ♂.

2. *Hussa.*—Cataract beginning in childhood and becoming advanced before old age (in one case at 40) ; 3 generations : I. ♀ cataract. II. 6 children of I, the 1st and 2nd ♂ and 4th ♀ affected, 3rd and 6th ♀ and 5th ♂ free. III. (*a*) 8 children of II, 1, the 1st, 2nd and 3rd ♂ and 5th ♀ affected, 4th, 6th and 7th ♀ and 8th ♂ free. (*b*) 5 children of II, 4, 1st ♀ and 3rd ♂ affected, 2nd ♂, 4th and 5th ♀ free. (*c*) 4 children of II, 6 (herself free), 1st ♀ and 4th ♂ affected, 2nd ♂ and 3rd ♀ free.

3. *Ira Smith.*—Cataract beginning about puberty, but not becoming dense till about 60 ; spontaneous improvement of V in some ; glaucoma in some. 3 generations : I. Both parents free. II. 6 children of I, the 1st ♂ 2nd ♀ and 6th ♂ cataract, 3rd and 5th ♀ and 4th ♂ free. III. (*a*) 7 children of II, 2, 1st and 5th ♀ cataract, Nos. 2, 3, 4, 6 ♂ and 7 ♀ free. (*b*) 4 children of II, 6, 1st ♀ cataract, 2nd and 3rd ♂ and 4th ♀ free.

Case 1 may be compared with my Case 97 in regard to the large proportion affected. Dr. Wood points out that I have omitted to mention some cases in American literature ; two of these (Millikin and A. D. Williams) and a third (Green, of St. Louis, not mentioned by Dr. Casey Wood himself) are given in the present paper ; Hansell's case, which seems important, I knew of, but have been unable to see the original.

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(The numbering is continued from the list at p. 246.)

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55. 1904. Millikin. American Journ. of Ophth., 1904, p. 74.
56. 1891. Schnabel. Ü. Cataracta der Kinder. Wiener Med. Wochenschr., 1891, No. 4.
57. 1896. Nolte (Fritz). Beitrag z. d. Lehre v. d. Erblichkeit v. Augenerkrankungen. Inaug. Diss., Marburg, p. 13 *et seq.*
58. 1889. Kunn. Vererbung d. Schichstaars in einer Familie. Wien. klin. Wochenschr., 1889, No. 3.
59. 1893. Fromaget. Gaz. hebd. d. Sc. Méd. de Bordeaux, 30 Juillet, 1893, p. 368.
60. 1892. Zirm. Klin. Monatsbl. f. A., 1892, p. 5 and p. 40 (January). (Erroneously named *Ziem* as Case 47 in my previous paper.)
Bergmeister. Additional particulars of same family communicated by letter.
61. 1890. Guiot. Année Méd. de Caen, 1890, vol. 15, p. 264.
62. 1900. Pisenti. An. d'Oculist, 123, p. 354, 1900.
63. 1880. Williams, A. D. St. Louis Medical and Surgical Journal, April 5, 1880.

EXTENSIVE CONGENITAL OPACITY OF RETINA IN YELLOW-SPOT REGION OF BOTH EYES. ? OPAQUE NERVE-FIBRES. HIGH MYOPIA ALSO PROBABLY CONGENITAL. CASE UNDER NOTICE 15 YEARS.

By E. Nettleship.

(With Plate I.)

In this case the difficulty is to interpret the ophthalmoscopic appearances; the coloured plate renders any lengthy description unnecessary. In each eye an oval area of the retina extending from the temporal side of the disc up to, and somewhat beyond, the yellow-spot, is opaque and white. The upper and lower borders of the patch and the part of it attached to the disc are fairly well defined and so dense as to entirely hide the choroid, but on the central part of the oval and at its temporal end the opacity is thinner and allows more or less of the choroidal red to shine through; but there was never any clear spot at the fovea centralis. The opacity is finely striated in the direction of the normal nerve-fibres of the region; the retinal vessels covered by the opacity in some places, superficial to it in others; at the temporal end of the affected area the choroid can be dimly seen to be mottled with ill-defined pigment spots between which it appears to be somewhat thinned (yellowish instead of the normal red). At the upper border of the o.d. the opacity disappears insensibly into a well-marked white scleral ring with pigmented border. The appearances were the same in the two eyes, but in the L. whilst the upper border of the opaque area was as dense as in the R. the lower border was thinner and less defined. In all other respects the fundi were perfectly healthy and showed no ordinary myopic changes.

In the first note, taken when the patient was 5 years old,

I compared the opacity to retinal embolism: four years later when she was 9 the drawing was made and my note ends with "the appearances are very similar to opaque nerve fibres." I do not think there had been any alteration between the two dates, but the first examination was less satisfactory than the second.

I saw this girl repeatedly between August, 1886, when she was 5, and January, 1900, and she was seen twice after that date by Mr. Holmes Spicer, who has kindly given me his notes and a sketch of the R. fundus that he made on the last occasion, January, 1902, when the patient was between 20 and 21. The following is a summary, omitting the description of the fundus already given :—

1886. August, æt. 5. Shadow test shows My. about 16 D. with a little As. in each eye; ophthalmoscopic estimation gives My. about 27 D. V. of R. (or better) eye not noted; with L. spells 14 J.

1888. January. Careful ophthalmoscopic note. Milk teeth all still present and good.

1891. May, æt. 9. Drawings of both fundi made by Miss Stone. (Plate I represents the R. eye.) Refraction by retinoscopy; R. My. 20 D.; L. My. 19 D.; no As. in either. R. – 18 D. sees 3/36, L. – 15 D. 3/60; no note of near vision. Ordered spectacles for distance R. – 16 D.; L. – 13 D.

1891. December, V. both eyes together with the above spectacles 3/60 to 3/36. Unaided reads 1 J. very close, and about 6 J. at 3 to 4 inches. Reads a good deal and makes no complaint.

1892. November. Reads much, and even small print, always without glasses. Chooses – 18 or 20 D. with each eye, and with such lens sees 4/60 with both together. Thin and pale; teeth have been troublesome lately.

1895. January, æt. 13. V. both together with – 20 4/60. Colour vision (wool test) normal. Choroid at and near the temporal end of the affected area in each is perhaps more patchy than when drawings were made.

1898. January, reads 2 J. with R. Mr. Donald Gunn finds some vacuoles and other small opacities in each lens, more

in L., and slight opacities in vitreous. Details at y.s. in R. seen with −25 D., and in L. with −28 D. (I have no earlier note of careful examination of the lenses, and some opacities may have been present from the first.) Has just passed the matriculation examination of the University of London, and is ambitious to teach mathematics. Question of removal of L. lens considered.

1899. January. Lenticular opacities somewhat increased; they take the form of dotted radii at posterior cortex and are most pronounced at nasal side; opacities in vitreous not increased; appearances of choroidal atrophy at y.s. rather more marked.

1900. January. All as last time; no increase of lenticular opacities.

1902. January, æt. 20 to 21. Mr. Holmes Spicer made a sketch of R. fundus and described the retinal opacity as having all the ophthalmoscopic characters of opaque nerve-fibres; through the thinnest parts he saw appearances of a large area of superficial choroidal atrophy; there was also a patch of choroidal atrophy above the o.d. away from the opaque retina and evidence of sclerosis of some of the choroidal vessels. The opacities in the lenses may have increased, for they now somewhat obscured the fundus, and with the R. (better) eye she read 4 J. at 3 inches instead of 2 or 1 J.; L. still read 12 J. as at the first examination, and V. of both together with −20 D. was still 4/60, as it was with same lens when she was 9 or 10 years old (1891 and 1892).

Subsequently she went as a teacher to Germany. She was independent in her habits, disliking assistance, and this led to her death by an accident when walking alone in the autumn of 1905, at the age of 25.

If the retinal opacity in this case was not due to ordinary congenital opacity of the nerve-fibre layer, can any other explanation be given? One knows of no other congenital condition producing such appearances, and the tolerably good vision in the better (R.) eye proved that the deeper layers of the retina were in good condition. On the other hand, the opacity occupied the macular region, which is supposed never to be subject to this peculiarity; it was more exactly

symmetrical and more nearly equal in quantity in the two eyes than in most cases of opaque nerve-fibres; some choroidal change was certainly present beneath the opacity when she was only 9 years old, and although this had become more marked by the time she grew up it was still almost confined to the area underlying the altered retina and was not associated with ordinary myopic changes. It is difficult to suppose that the opaque area represented an abrupt and steep-sided, macular staphyloma; but such a condition cannot be quite excluded, because no comparative estimation of the degree of the myopia at the y.s. and elsewhere was ever made. Although, as already stated, the comparatively good vision of the R. eye disproved any very serious affection either of the percipient or the conducting elements of the retina, the appearance of more or less choroidal change quite early in life in both eyes, together with the much higher amblyopia of the L., in which nevertheless the retinal opacity was somewhat less, may point to the whole process having started in the choroid in fœtal life and caused not only the protrusion indicated by the myopia but secondary changes in the retina. It must be admitted, however, that this explanation is purely hypothetical. The lenticular opacities had little or no share in causing the defect of sight.

Family history. The patient was the youngest of a childship of eight, was born at full time when her mother was 39 or 40, was suckled, and never in her life had an important illness. There were in all 10 pregnancies in 16 years; the third and one other ended in miscarriage, the other 8 gave living children of whom all except the subject of this paper are still alive (1906), healthy and with normal sight (except anisometropia in the second, see below). There was an interval of 3 years between No. 7 and No. 8 (the patient). From the history it is probable that the mother had heart disease for some years before the patient's birth. The second child, a boy 11 years her senior, was examined at Moorfields when he was eighteen; he had slight

H. in the right eye, My. 2 D. in the L., V. of each being full with correction. The patient's father and mother were not myopic, but two of the father's sisters and their mother were said to have been so. The father is living and well (1906); the mother, who had cardiac disease, died about 1896, aged 54.

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EHRLICH'S THEORY OF IMMUNITY IN ITS RELATIONSHIP TO OPHTHALMOLOGY.

By J. Herbert Parsons.

The investigation of the processes which underlie the various forms of immunity to the action of toxic agents in the body has led to far-reaching results which have an important bearing upon nutrition, not only in its pathological, but also in its physiological manifestations. The researches of Metchnikoff and his colleagues at the Pasteur Institute and of Ehrlich and his followers have thrown a flood of light upon cell-life, and though the subject is one of great complexity it can no longer be ignored in dealing with the problems of physiology and pathology. It is only recently that the influence of the theory of immunity has made itself felt in the domain of ophthalmology, almost entirely owing to the researches of Römer, himself a pupil of Ehrlich. In order that the relation of immunity to ophthalmic problems may be comprehensible, it is necessary to give a brief account of the evolution of the theory, more particularly as enunciated by Ehrlich.

The fundamental peculiarity of living cells is the elective affinity which they exhibit for certain substances which are useful for their nutrition; the substances varying with the type of cell. Chemical and physical processes have hitherto failed to give a satisfactory explanation of this peculiarity. It is well known that synthetic processes occur in the metabolism of the cell. Substances which are available for the nutrition of the cell must be such as are capable of being assimilated and synthetically bound up in the cell. In order that this may occur chemical groups must exist in the cell and in the food stuff which possess strong affinity for each other. These chemically active groups in the living

protoplasm, which have a maximal affinity for definite groups in the food substances and which serve to anchor the latter to the cell, are called by Ehrlich *side-chains* of the protoplasm or *receptors*. According to the side-chain theory the specific nutrition of individual types of cells is due to the possession by the living protoplasm of atom complexes which are capable of linking on certain other atom complexes, thus adding them to the protoplasmic molecule.

The side-chain theory is founded upon the analogy of the benzene ring, in which, by the linking on of other chemical groups, the character of the substance is entirely changed, though the benzene nucleus remains intact. Ehrlich first expounded the theory in 1888, in a book upon the need of the organism for oxygen.

Antitoxins.—Ehrlich's fundamental proposition found its earliest and most important application in explaining the production of antitoxins. Antitoxins had already been prepared by methods which were almost entirely empirical; the *rationale* of their formation was merely a matter of conjecture. Their origin, and the enormous quantities which it was possible to obtain in small volumes of serum, had not yet been satisfactorily explained. It was natural to suppose that the toxin was directly transformed into antitoxin, but this failed wholly to account for the quantities produced. Their most striking feature was their specific activity. Diphtheria antitoxin protected only against diphtheria, tetanus antitoxin only against tetanus. This characteristic especially pointed to the direct transformation of toxin into antitoxin, a view which was held by Buchner and Metchnikoff. Facts which militated against this theory rapidly accumulated. Some of the more striking may be mentioned. Thus, one part of toxin might give rise to 100,000 parts of antitoxin (Knorr). An animal might be deprived of nearly the whole of its blood by bleeding, but after a short interval the antitoxin content of the newly formed blood had reached its former level (Salomonsen and Madsen, Roux and Vaillard). Moreover, antitoxins are

present in the blood of quite normal animals, *e.g.*, diphtheria antitoxin and tetanolysin antitoxin in horses, staphylotoxin antitoxin in man, etc. Everything pointed to the fact that antitoxin production was a function of the living organism.

The investigations were first put upon a sound basis by Ehrlich's experiments with ricin and abrin. These poisons when administered to animals lead to the production of specific antitoxins, and Ehrlich succeeded in obtaining accurate quantitative estimates of the relationship between the dose of poison and the degree of immunity. From his experiments Ehrlich was led to apply his side-chain theory to the explanation of the problem. The bacterial poisons are substances which nearly approximate to proteids in their chemical constitution. Individual poisons possess atomic groupings which correspond with those of certain food substances. When such a poison is introduced into the body the possibility arises of the toxin entering into direct chemical relationship with the protoplasm of suitable cell-types. If the toxin possesses groups which are identical with those of the food stuff, it will become chemically anchored to the protoplasm. Ehrlich went a step farther, enunciating the essential axiom of the theory of immunity. Directly the toxin is anchored to a receptor the latter can no longer fulfil its physiological function. If the function of the cell is not so severely affected as to cause the death of the cell, its protoplasm possesses the capacity of replacing the disabled side-chain. Not only so, over-compensation occurs, and more receptors are formed than are essential to the metabolic functions of the cell. This is especially the case when the stimulus is repeated, as is effected in immunisation by renewed doses of toxin. Finally, a time is reached when so many receptors are produced that they form an encumbrance to the cell. They are then cast off into the blood. Since they still retain the atom-complex which enables them to anchor the toxin, they now act as antitoxin. In the words of v. Behring, "the same substance in the living body, which, when present in the cell, is the

postulate and condition of poisoning, becomes the cause of cure when circulating in the blood stream."

The next problem to be solved was the nature of the action of the toxin upon the antitoxin. If a certain dose of diphtheria toxin in bouillon is injected into a guinea-pig, the animal dies with characteristic symptoms. If previously a sufficient dose of antitoxin has been injected, the animal remains healthy. The same result occurs if the toxin and antitoxin are mixed before injection. No change is seen to occur in the serum when the mixture is made. An antitoxic serum is apparently exactly like a normal serum; indeed, v. Behring has shown that the antitoxin is absolutely harmless.

The first proof that the action of the antitoxin upon the toxin is a direct chemical combination, was shown in Ehrlich's experiments with ricin. More striking perhaps were the later experiments of Martin and Cherry with diphtheria. If a diphtheria serum is passed through a gelatinised Pasteur-Chamberland filter it loses its antitoxic character. Diphtheria toxin, on the other hand, passes through such a filter with little loss of toxicity. If therefore a mixture of the two be passed through the filter, we may expect the filtrate to be toxic if the mixture is merely a mixture of the toxin with the antitoxin, whereas if the two have entered into chemical combination they may be expected to pass through intact. Martin and Cherry showed that the filtrate was absolutely innocuous.

The same investigators have proved by another method that chemical combination occurs. If Calmette's antitoxin to snake poison is warmed for 10 minutes it ceases to be antitoxic; the same treatment has no effect upon the poison itself. Mixtures of the toxin and antitoxin were kept for 30 minutes at 20° C. After warming to 68° C. the mixture was found to be quite innocuous.

These and other such experiments prove also that the combination of the toxin with the antitoxin is independent of the organism, since it occurs equally well *in vitro*.

Further, as in all chemical combinations, the law of multiples obtains. If 1 c.c. of antitoxic serum suffices to neutralise 100 lethal doses of poison, 3 c.c. will render 300 such doses inactive (v. Behring, Knorr, Ehrlich, Cobbet and Kanthack, Römer).

These researches negative the Roux-Buchner theory that the antitoxin has no direct action on the toxin but acts upon the cells. Römer has confirmed the results in the actual presence of living cells by using the conjunctival sac as a test-tube. If a drop of jequirity solution is instilled into the conjunctival sac, the abrin contained in it causes the development of a croupous conjunctivitis after a short incubation period. If on the other hand a mixture of abrin solution and antitoxin, in such proportion that the toxin is neutralised and anchored to the antitoxin, is instilled, the eye remains as quiet as if physiological salt solution had been used. If the slightest excess of toxin is present inflammation results. Römer has elaborated the principle so as to afford a new method of quantitatively estimating the interaction of abrin and antiabrin. It may be pointed out that an animal cannot be immunised by such a neutral toxin-antitoxin mixture, since all the toxin is rendered ineffective, not only for causing an inflammatory response, but also for stimulating the over-production of receptors which is the basis of immunity. The same mixture is neutral to any animal, whether injected into a mouse, instilled into the eye of a rabbit, or injected into the circulation of the highly susceptible guinea-pig.

From the clinical standpoint antitoxin has a double *rôle*—prophylactic and curative. The prophylactic effect is comprehensible on Ehrlich's theory from the circulation of large quantities of unsatisfied receptors in the blood circulation. The curative effect is less easily understood. According to Metchnikoff the process is not brought to an end by the mere combination of toxin and antitoxin. The leucocytes are supposed to play an important part in making the organism proof against the toxin. The union of toxin with

antitoxin simply raises the value of the toxin as a food material for the leucocytes. According to Ehrlich, however the curative effect of the antitoxin is due to the ability of the antitoxin to dissociate the toxin from combinations which it has already made with the tissues of the body. As an example the curative effect of tetanus antitoxin may be cited. Dönitz has shown that tetanotoxin is immediately taken up from the blood by the tissues, so that when a large amount is injected the lethal dose is fixed in four to eight minutes. The anchored poison is dissociated from the tissues by the antitetanus serum, is forthwith neutralised and rendered innocuous. The dissociation is the more difficult the longer the interval between poisoning and the introduction of the serum. Although the toxin is fixed by the cells in a few minutes, yet cure may be effected after 30 minutes by the administration of five to ten times the neutralising dose of antitoxin. After a longer interval the strongest dose of antitoxin fails to save the animal.

Römer's experiments with abrin are of special interest to the ophthalmologist in this connection. By the administration of antiabrin the inflammation produced by jequirity can be controlled. Not only is any free abrin which may be present neutralised, but that already combined with the tissues is set free and neutralised. Even more striking is the fact that the application need not be local to the conjunctival sac, for subcutaneous, intravenous, or intraperitoneal injection effects the same result. Here it is obvious that the antitoxin circulating in the blood and lymph has the capacity of attacking the toxin fixed by the cells.

Careful consideration of the mode of action of organic toxins affords suggestive inferences as to the structure of the toxin molecule. Three features stand out prominently, viz., the specific activity of the toxin, its capacity to give rise to antitoxin, and the existence of an incubation period. The last fact emphasises the difference of toxins from most chemical poisons. For example, even if tetanotoxin is injected directly into the brain, the cells of which show

a special avidity for it, yet a definite latent period occurs before poisoning sets in (Roux and Borrel). To explain this peculiarity, Ehrlich conjectures that every toxin molecule contains two different chemical groups, a haptophore group and a toxophore group. The *haptophore group* subserves the combination of the toxin molecule with the cell, which for its part possesses a complemental unsatisfied group, viz., the receptor. The *toxophore group* is the noxious element, which cannot exert its influence until linked on to the cell through the mediation of the haptophore group. On the side-chain theory the two groups are otherwise essentially independent.

The effect of the simpler chemical poisons, *e.g.*, alkaloids, upon the cell is rapid and short-lived. The effect of organic toxins is slow and prolonged. They induce metabolic changes which modify the whole life-history of the cell; hence the analogy which Ehrlich delineated between their activity and cellular nutrition. Indeed, the analogy is very striking, especially when viewed in the light of Emil Fischer's experiments on ferment action. The activity of ferments is conditioned by the possession of a definite atomic grouping, which shows a specific avidity for a complemental grouping in the substance attacked. Only such substances as possess the complemental group are subservient to the activity of the ferment, just as a lock can only be opened by a certain key. Further analogies are found in the physiological activity of definite atomic groups in synthetic hypnotics, anæsthetics, etc., *e.g.*, the ethyl group is prepotent in hypnotics, the benzoic acid group in anæsthetics.

As regards the toxophore group, its enormous toxicity is noticeable: 0·0000004 gramme of the tetanus poison is the lethal dose for a mouse. The next most notable feature is its lability; slight influences suffice to attenuate its activity. Most striking in this respect is the fact that the attenuated virus does not lose its capacity for producing antitoxin. Hence Ehrlich hypothecated a second, stable, haptophore

group in the toxin molecule, and it is this group which not only conditions the anchoring of the toxin to the cell, and so activates its toxicity, but also subserves the production of the antitoxin. This is shown by the fact that toxins whose haptophore groups are satisfied by antitoxin are no longer suitable for immunisation; they have lost their capacity for inducing the formation of antitoxin.

The experimental proof of the existence in the toxin molecule of two different groups was given by Morgenroth. He made use of the discovery by Courmont and Doyon (1892), that the frog, although insusceptible to tetanus at the ordinary temperature, became affected if kept at a raised temperature. This might be due to one of two causes: either the toxin did not become anchored to the nerve cells at the lower temperature, or, though anchored, the toxic element was not capable of acting at this temperature. That the latter was the true explanation is shown by the fact that the longer the animal was kept in the cold after injection of the toxin, the more antitoxin it was necessary to inject in order to protect it from tetanus on warming. Moreover, the same fact was confirmed by observation of the incubation period. Thus, the usual incubation time after raising the temperature is two to three days. Morgenroth kept frogs for 24 hours at 32° C., and then replaced them in the ice chest for days or weeks; on again warming them tetanus supervened after an incubation period which was never shorter than the normal by more than 24 hours. In other words, the cold interval was simply intercalated; on warming, incubation went on exactly from the point at which it had been stopped. Hibernation has exactly the same effect (Billinger, Dönitz). The presence of two groups in the toxin molecule has also been shown by Neisser and Wechsberg's researches on staphylolysin, the poison formed by the staphylococcus which has the power of dissolving the hæmoglobin out of red corpuscles.

The facts and theoretical considerations which have hitherto been discussed apply to those toxins which are

secreted by bacterial organisms and cast off into the surrounding medium, *e.g.*, diphtheria, tetanus, etc. There are other pathogenic organisms which do not excrete the whole of their poisons but keep them locked up in their own tissues, *e.g.*, typhoid, cholera, plague, etc. Here the action of antitoxins is different and more complicated, but it is probable that they act as specific bactericidal agents. Two early hypotheses as to the cause of immunity in these diseases may be quickly dismissed. It was considered probable that the organism during the first attack used up all the available nutrient material, which it was supposed must be of a specific nature. Another view was founded on the fact that bacteria produce excretion products which have an inhibitory effect upon their own growth. As was proved by Flügge and his pupils, however, there is no evidence that any such products are retained indefinitely in the body. Finally, Metchnikoff attributes to the leucocytes the *rôle* of destroying the bacteria by ingestion.

In 1896 an important observation was made by Pfeiffer. If a subminimal lethal dose of typhoid bacilli, or a dose of bacilli mixed with serum from an immunised animal, is injected into the peritoneal cavity of a guinea-pig, and specimens of the peritoneal exudates are examined under suitable conditions, it will be found that in a few seconds after injection the bacilli have lost their motility. Moreover they rapidly undergo changes in appearance. The bacteria become swollen and break up into granules, which soon dissolve entirely in the fluid, so that the number of organisms quickly diminishes. According to the Ehrlich theory this phenomenon is due to the presence of antitoxins in the fluid, though this is denied by Metchnikoff.

The analogy of the breaking up of bacteria to the well-known breaking up of red corpuscles under certain circumstances, led to the latter phenomenon being carefully studied from this standpoint. There can be no doubt that the least exceptionable evidence in favour of Ehrlich's theory is to be

found in the beautiful experiments which have been made on hæmolysis.

Hæmolysins.—It has long been known that the serum of many animals has the power of dissolving the hæmoglobin out of the red corpuscles of the blood of other animals, especially if the latter belong to a quite distinct species. The subject was investigated by Landois, and is responsible for the abandoning of blood transfusion. In 1898 Belfanti and Carbone showed that the serum of horses became much more toxic to rabbits if rabbits' blood had been previously injected into the horses. Bordet attributed this to the formation of specific hæmolytic substances. He injected repeatedly 3 to 5 c.c. of defibrinated rabbit's blood into the peritoneal cavity of a guinea-pig; the serum of this animal rapidly dissolved the hæmoglobin out of the red corpuscles of rabbit's blood *in vitro*, though normal guinea-pig's serum has little or no such power. Confirmatory experiments by Landsteiner and v. Dungern and others proved the extraordinary specificity of the reaction. It may be stated, as a general rule, that if the red corpuscles of one species are injected subcutaneously, intraperitoneally, or intravenously into another species the serum of the latter—"immunised"—animal becomes toxic to the erythrocytes of the former animal. It is clear that differences in osmotic pressure fail to explain the phenomenon, since a fraction of a milligram of serum cannot alter the tonicity of the fluid, as may indeed be proved by adding it to an isotonic saline solution. According to Ehrlich, hæmolysis is the sign of protoplasmic death in the stroma of the erythrocytes. It is usual to speak of the escape of hæmoglobin as solution of the blood cells, though the stroma is not destroyed.

Further experiments showed that the analogy between antitoxins and hæmolysins extended to their chemical behaviour. Bordet found that if fresh hæmolytic serum was warmed to 55° C. and kept at this temperature for half an hour it became inactive. If a small quantity of normal guinea-pig's serum, which is also hæmolytically inactive,

was added to this inactive serum it again became hæmolytic to rabbit's blood. Hæmolysis is therefore due to the presence of two substances, one of which is present preformed in the animal's serum, whilst the other is formed by the process of immunisation. Bordet called the thermostable element substance sensibilisatrice; it has since received many other names—preparator (Gruber), helping body (Buchner), copula (P. Müller), desmon (London), philocytase or fixator (Metchnikoff), immune body or between body (Ehrlich and Morgenroth). Ehrlich has finally settled on the name *amboceptor*, which has been generally adopted. Bordet thought that the thermolabile substance was identical with Buchner's alexin, which is a substance in serum acting upon bacteria and foreign blood corpuscles like an enzyme. It has since been called addiment or finally *complement* by Ehrlich, and cytase by Metchnikoff.

It has already been mentioned that hæmolysins are specific. Thus, rabbit's serum immunised for guinea-pig's blood is only active to guinea-pig's erythrocytes; it will not dissolve sheep's erythrocytes. From this fact Ehrlich concluded that either the amboceptor or the complement possessed a specific affinity for some atom-complex in the red cell. Ehrlich and Morgenroth proved it in the following manner:—A goat was immunised by injection of sheep's blood. The serum was warmed at 55° C., so that the complement was destroyed. One cubic centimetre of this inactive serum was added to 4 c.c. of 5-per-cent. sheep's blood; the mixture was kept at 40° C. for 15 minutes and then centrifuged. To the clear fluid 0·2 c.c. of normal sheep's blood and 0·8 c.c. of normal goat's blood were added, and the mixture was kept at 37° C. for two hours; not a trace of solution occurred. The sediment from the centrifuging was then washed in 4 c.c. of 0·85-per-cent. salt solution, and 0·8 c.c. of normal goat's serum was added; in two hours there was complete solution. The experiment proves that the amboceptor was absorbed by the red

corpuscles; only on the addition of a small quantity of normal serum containing the complement was solution obtained. It was not, however, a simple absorption, for if so, other red corpuscles might be expected to serve the purpose equally well. This was not the case; hence, there is a definite specific chemical combination. The corpuscles can be repeatedly washed with physiological saline solution without causing any dissociation of the amboceptor from the cells. Quantitative experiments show that the amount of amboceptor anchored varies in different cases.

Ehrlich concludes from these experiments that the amboceptor possesses a haptophore group by means of which it becomes anchored to a receptor in the cell.

Corresponding experiments with the complement showed that this is not taken up by the corpuscles. Investigations carried out at different temperatures showed that the haptophore group of the amboceptor united with the receptor of the erythrocytes in the cold, whereas its affinity for the complement is less, and is only manifested at a higher temperature. It must, therefore, possess another haptophore group which is complementophile. Since the union of the complement can only be carried out by means of the cytophile and complementophile groups of the thermostable substance, this was suitably called the amboceptor. It finds its analogy in organic chemistry in diazobenzaldehyde. The analogy between a hæmolysin and a toxin scarcely requires to be pointed out; the haptophore group of the toxin is represented by the amboceptor, the toxophore by the complement. Bacterial hæmolysins have been described for pyocyaneus (Bulloch and Hunter), for streptococci (Basredka and Marmorek), for diphtheria (Lubenau), for typhoid (E. and P. Levy), etc. Snake poisons also contain hæmolysins (Stephens and Myers, Flexner and Noguchi).

It is unnecessary here to enter into the much-disputed question of the site of formation of the antitoxic and hæmolytic constituents. The specific nature of the ambo-

ceptor and the multiplicity of complements may be mentioned. The similarity of the complement to a ferment is emphasised in Metchnikoff's name—cytase. There is a striking parallel in the *rôle* of enterokinase in digestive processes and that of the complement in hæmolysins. It is not improbable that this fact may point the way to some general law of wide applicability, which will evolve order out of the chaos of these and similar difficult problems of physiology.

Neither is it necessary here more than to mention that hæmolysins may, under suitable conditions, give rise to antihæmolysins. Isohæmolysins, and autohæmolysins, or bodies which cause solution of the hæmoglobin from the cells of the animals of the same species or of the same animal, have also been described; they, too, give rise to antibodies. Their importance can scarcely be exaggerated, but little is yet known about them.

The facts of hæmolysis have been utilised by Römer in attacking two problems of ophthalmology—one therapeutic, the other pathological. In the former hæmolysins have been injected into the vitreous in cases of intraocular hæmorrhage with a view to assisting in breaking up the red cells and promoting absorption. In some cases the results have been favourable, but in others necrosis of the tissues has shown that the method is not without danger (Elschnig).

By the aid of hæmolysins Römer has brought forward the most delicate evidence against the ciliary nerve theory of sympathetic ophthalmia. According to this theory the irritation of the ciliary nerves in the exciting eye causes a sort of symmetrical irritation of the ciliary nerves of the other eye, so that the way is prepared for the sympathetic inflammation. If such irritation occur it is to be expected that it will manifest itself by increased hyperæmia of the ciliary body, and this will be followed by the transudation of a more highly albuminous lymph than normal. Wessely investigated the problem by estimating the amount of proteid in the aqueous of each eye after one had been

irritated severely. He found no increase in the second eye, and his results have been confirmed by Tornabene. Such experiments to decide so delicate a point are too crude to be of much value, since the error of experiment is probably fully as large as any alteration which might be reasonably anticipated. The hæmolysin test is far more delicate. Römer first confirmed the observation of earlier investigators that no hæmolysins are present in the aqueous of immunised animals, *e.g.*, if a rabbit is immunised against ox corpuscles by the injection of 15 to 20 c.c. of ox blood into the peritoneal cavity, the rabbit's aqueous will not dissolve ox corpuscles. If, however, the aqueous is drawn off a second time after an interval of three-quarters of an hour it is powerfully hæmolytic. The delicacy of the test is shown by the fact that a milligram of the second aqueous will dissolve 50 or 60 million red corpuscles. Now, intense irritation of one eye does not cause the slightest trace of hæmolysin to appear in the normal aqueous of the other eye, whilst in every iritis and iridocyclitis, no matter how slight, hæmolysins are at once found in the aqueous of the first eye.

It was possible that the complement might already be present in the normal aqueous, whilst perhaps only the immunising body, the amboceptor, which in serum is chiefly attached to the globulins, entered with the regenerated aqueous. An exactly titrated hæmolytic serum was heated to 60° C: hæmolysis only occurred if 0·01 active normal serum, containing the complement, was added to 0·0008 c.c. of this, which contained the amboceptor. It was found that even 0·2 c.c. of first-drawn aqueous added to 0·0008 c.c. of the inactive immunised serum failed to cause hæmolysis. The complement was therefore not already present; it only appeared when the aqueous was regenerated. It was similarly proved absent from the first aqueous of the immunised animal. In an analogous manner it was also proved that the amboceptor was not already present in the first aqueous of the immunised animal. After puncture the

complement appeared in the aqueous of the normal animal, and also the amboceptor in the immunised animal.

Römer further showed that the complement was present in the aqueous one hour after subconjunctival injection of 4 per cent. salt solution.

One eye was irritated by various means—a chip of copper in the anterior chamber, injection of dead typhoid bacilli or staphylococci into the vitreous, etc. In every case the first aqueous was hæmolytic in the injured eye but not in the other. The same result followed chronic intraocular inflammation caused by the injection of a non-pathogenic culture of bacillus subtilis. Further, although the second aqueous of the uninjured eye naturally contained hæmolysins, these disappeared in 24 hours. The experiments were also confirmed on monkeys immunised with ox-blood.

Bacteriolysins.—Reference has already been made to Pfeiffer's experiment (*vide* page 47). It is not my intention to enter into details as to the mechanism of bacteriolysis, nor into the cognate question of bacterial immunity. It will be remembered that it is a matter here of organisms such as typhoid, cholera, plague, pneumonia, etc., which exert their main influence, not by virtue of excreted toxins as do the tetanus and diphtheria bacilli, but by noxious properties contained in themselves. The subject is of enormous importance in the whole range of medicine, but chiefly from the prophylactic and therapeutic points of view.

It seems certain that the injection of dead cultures of the type of organism under consideration produces a definite reaction whereby the leucocytes are stimulated to increased bacteriolytic activity. The chemical stimuli which produce this result have been called *opsonins* by Wright.

It may be mentioned in passing that Römer has instituted a campaign in this field also. It has already been pointed out that the majority of cases of ulcus serpens are due to the pneumococcus. Statistical researches show that more than half the accidental wounds of the eye

eventuate in ulcus serpens (Römer). Römer has shown that the eye can be protected against pneumococci by immunisation. As a prophylactic method the results are perfect in rabbits; as a curative method they are successful if the remedy is applied early. The immune serum is best obtained from rabbits, even when used for man. Römer maintains that early immunisation by antipneumococcic serum in man protects against the development of ulcus serpens, and that even progressive hypopyon ulcers can be brought under control.

Agglutinins, Precipitins.—Agglutinins, which have an ætiological importance in general medicine, and precipitins, which bid fair to assume a preponderant *rôle* in forensic medicine, have not hitherto given evidence of much importance in ophthalmology. It is sufficient to mention here that, while receptors of the first order, such as serve to anchor toxins, ferments, and other cell secretions, possess only one haptophore group, those of the second order, which serve to bring about agglutination and precipitation, possess a haptophore group and a zymophore group. Agglutinins and precipitins pass readily into the aqueous; hence they are doubtless innocuous and are probably valuable as food material.

Cytotoxins.—The discovery of substances having a specific destructive influence upon red corpuscles naturally led to investigation as to the existence of specific poisons for other types of cells.

v. Dungern injected ciliated epithelium from the trachea of the ox into the peritoneal cavity of the guinea-pig. He found that the cells retained movement in their cilia for two days; in a week or so all the cells have disappeared. A fresh dose of epithelium was injected 10—12 days later. In 18 hours all the cells had disappeared. Hence the animal had acquired a distinctly increased power of destroying the cells. Further research brought out the interesting fact that the serum of animals immunised against ciliated epithelium of the ox was hæmolytic to ox-red corpuscles.

Hence ciliated epithelium and erythrocytes must possess the same or nearly allied receptors. Even the injection of milk into a rabbit produced a serum which contained cytotoxins to ciliated epithelium and hæmolysins to ox-blood.

An immense amount of work has been done on the same lines with spermatozoa by Metchnikoff and his pupils and others (Landsteiner, Moxter). The spermotoxic serum is also hæmolytic. On the other hand, Metchnikoff has shown that a hæmolytic serum produced by injection of blood is not spermotoxic, whilst the spermatozoa in a serum produced by simultaneous injection of spermatozoa and blood possesses the capacity of anchoring both the hæmolytic and the spermotoxic amboceptors.

Delezenne and Centanni have produced neurotoxins by the injection of brain substance. Many other cytotoxins have been investigated, *e.g.*, liver (Delezenne, Schütze, Deutsch, Hulot and Ramond), kidney (Bierry, Lindemann, and others), placenta—synzytiotoxin (Ascoli and others), ovary (Ceconi and Robecchi), suprarenal (Bigart and Bernard, Sartirana), pancreas (Surmont, Carnot, Garnier), stomach (Théohari and Babès, C. Bolton), pituitary body (Collina), thyroid (Gontscharnkoff, Mankowski, Sartirana).

More interesting to ophthalmologists are the conjectures of Römer as to the cause of senile cataract deduced from the side-chain theory. He compares the lens to a red corpuscle, each having a surrounding membrane which impedes the diffusion outwards of important constituents. When the hæmoglobin has passed out of the erythrocyte the cell is dead; so, too, cataract is the expression of the protoplasmic death of the lens fibres. Previous observations in hæmolysis have shown that isohæmolysins can be formed, *e.g.*, in the goat (Ehrlich and Morgenroth); autohæmolysins, on the other hand, are only formed under pathological circumstances. If autocytotoxins occur it might be expected that they would be a sign of senile change, for atrophy and degeneration of tissues are the common features of old age.

Now it is necessary, if lentotoxins occur, that they should be able to reach the lens, or rather that the lens should be protected from them under normal circumstances. Hence the importance of knowing the behaviour of the secretory apparatus of the eye with regard to such bodies. It may be pointed out here that the essential feature of cytotoxin activity is its fixation by the cell; this has nothing to do with osmotic conditions, but as soon as the cell is poisoned osmotic processes will have free play.

It has already been mentioned that neither constituent of hæmolysin, neither amboceptor nor complement, is present in the aqueous either of the normal or the immunised animal. Receptors of the second order—viz., agglutinins (Metchnikoff, Wessely, Römer) and precipitins (Römer), pass freely through into the aqueous. These, however, do not act as cytotoxins, for the latter are always receptors of the third order, *i.e.*, amboceptors with two haptophore groups one cytophile, the other complementophile. Teleological considerations would lead one to suppose that substances of this type are not suited for nutrition of the lens and vitreous.

Römer has succeeded in showing that there are receptors of the second order in the lens. *i.e.*, such as possess a haptophore and a zymophore group, and may be distinguished by their agglutinative properties. He has further shown that there are receptors of the first order present, *i.e.*, such as possess a haptophore group which is capable of combining with substances of the type of toxins, ferments, and other cell secretions. He has also shown that there are complementophile receptors in the lens, and that these exhibit definite specificity. The experiments are too complicated for minute consideration here; they must be studied in the original communication. They tend, however, to support the theory that senile cataract is a result of the specific activity of lentotoxins.

Römer has recently investigated the question of retinal cytotoxins. Cytotoxins as a cause for cyclitis is a thesis

which has not yet been investigated, but would appear *a priori* to be specially likely to give affirmative results. These curiously insidious cases give every sign of toxic activity. In many cases a septic focus can be found in some part of the body, especially in the mouth—pyorrhœa alveolaris, etc. Here doubtless the cyclitis is the result of a bacterial toxæmia. In other cases in which no cause can be discovered it is not improbable that the essential factor is a specific cyclotoxin.

In my opinion, however, the work which has been done on cytotoxins in general is the weakest part of the structure which has been built on the basis of the side-chain theory. It is impossible at present to attempt to correlate the isolated facts which have already accumulated. It may be expected that further research, and especially the valuable criticisms and investigations of the Metchnikoff school, will eventuate in the discovery of some general principle underlying these complex problems.

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AN ANALYSIS OF A SERIES OF CONSECUTIVE CONJUNCTIVITIS CASES SEEN IN ABERDEEN.

By C. H. Usher and Henry Fraser, Aberdeen.

As no record exists of the micro-organisms which cause conjunctivitis in this part of the country, we were led to observe clinically and bacteriologically the cases on which this article is based, and in order to arrive at the relative frequency of such organisms, a series of consecutive cases was taken. Throughout the inquiry attention was paid to the question of how far, by means of clinical characters, a conjunctivitis caused by a certain micro-organism may be distinguished from that produced by other micro-organisms. In May, 1904, preliminary observations were commenced with a view to determine the methods which would best suit our requirements. Films from the discharge of various cases were made and examined. The growth of the different micro-organisms was the next consideration. A study of the literature showed that the diplobacillus of Morax and Axenfeld did not give rise to much difficulty in its cultivation. The Koch-Week's bacillus, on the contrary, appeared to require very favourable conditions for its growth. Axenfeld* states that for the growth of the diplobacillus blood-serum agar or medium mixed with human fluids should be employed. Agar mixed with one-third hydrocele or ovarian fluid is excellent. Ascitic fluid may also be employed. Morax† states that for the growth of the diplobacillus we must employ agar mixed with serum in accordance with Wertheim's method. Morax employed

* Centralblatt für Bacteriologie, January, 1897. Über die chronische diplobacillen conjunctivitis.

† Note sur un Diplobacille Pathogene pour le conj. humaine. Annales de l'institute Pasteur, 1896, p. 337.

ascitic fluid for this purpose. Morax and Bach state that the best medium is a mixture of human serum and agar.* We decided to commence with ascitic agar. The ascitic fluid was collected under aseptic precautions, a sterilised trochar and cannula with rubber tube attachment being used to withdraw the fluid. The first portions of the fluid were allowed to run off and then sterilised filter flasks were charged with the fluid. Both openings were closed in the usual manner with sterilised cotton wool. It may be remarked of fluids collected in this manner that they have remained aseptic for seven or eight months, notwithstanding that their amounts were constantly diminished by frequent use. A 2-per-cent. agar was employed, standardised to a reaction of + 10 phenolphthaleïn, which was placed in test-tubes and sterilised thereafter in the autoclave. At first the method recommended by Morax was employed. The agar was liquefied and cooled to 60° C., one-third part of serum was then added to each test-tube and carefully mixed. The tubes were sloped, and, when the mixture was solid, they were placed in the incubator for 48 hours to test their sterility. This process of cooling to 60° C. was soon found to be unnecessary. The tubes were placed in a water bath and the agar liquefied, the wool plug was removed from the lateral tube in the flasks employed for collecting the fluids, the lateral tube and the parts adjacent were then sterilised by means of a Bunsen flame, and the tubes of liquefied agar had then added to them the requisite amount of fluid. The contents of the tubes were carefully mixed, sloped and allowed to solidify. After preparation of a batch of tubes, the lateral tube was carefully wiped free of fluid by wool and thereafter replugged with cotton wool, and the lateral tube so plugged was sterilised by means of a Bunsen flame. This method has been employed for over 18 months, upwards of a dozen various fluids being used and more than 1,500 tubes of media prepared, without

* Quoted from Weichselbaum and Muller: Über der Koch-Weekschen Bacillen der acuten conjunctivitis. Arch. f. Ophthalmologie, 1898, p. 108.

in a single instance the fluids or media being contaminated. The ascitic agar furnished growths of the diplobacillus of Morax and the gonococcus, but it did not yield evident growths of the Koch-Week's bacillus. It was then decided to try ovarian fluid. On substituting this for the ascitic fluid during an epidemic of Koch-Week's conjunctivitis, beautiful colonies of the bacillus were obtained. Some of these were pure cultures which were subsequently sub-cultured through as many as 40 generations. Comparative cultures of the Koch-Week's bacillus so obtained on ascitic and ovarian agar did not show an appreciable difference in the appearance of their colonies, yet the growth on ovarian agar was more profuse, and on the whole much more satisfactory.

When sufficient experience had been gained in the recognition of various micro-organisms met with in the conjunctival sac and of the clinical conditions associated with these, a series of 100 cases, for the most part consecutive, was investigated. For this series a chart was devised, by the aid of which a clinical diagnosis of the organism present was made. In certain cases it was confirmed by the bacteriological examination, in others it was not. An analysis of the cases was made, with a view to determine the value of each of the clinical characters as an aid in forming a diagnosis, and so increase, if possible, the accuracy of a clinical diagnosis in a subsequent series. Some features seemed to be associated with certain specific micro-organisms. The reliability of these was again repeatedly tested on other cases before the commencement of an examination of a further series of consecutive conjunctivitis cases.

During the year 1905, all cases of conjunctivitis coming to the Aberdeen Royal Infirmary and Dispensary were examined. In order to bring the clinical characters of each case into line, for purposes of comparison, the following schedule was filled up in each instance at the time of examination :—

Date . Number of case .
Sex . Infirmary .
Age . Dispensary .
Aberdeen or .
Complaint—Gritty or similar feeling. Heavy lids.
Difficulty in reading. Gumminess of lids.
Rainbows. Other complaints.
Interval since onset of attack .
Previous attacks .
Others with sore eyes (1) in same house ; (2) elsewhere .
Colour of conjunctiva (*a*) palpebral ; (*b*) ocular .
Amount of discharge (1) none or very slight; (2) moderate; (3) profuse.
Character of discharge (1) purulent; (2) muco-purulent.
Follicles enlarged .
Conjunctival hæmorrhages .
Chemosis .
Membrane on conjunctiva .
Swelling of lids .
Preauricular gland enlarged .
Eye affected R. ; L. .
Corneal ulcer ; phlyctenules ; impetigo ; nasal discharge ; ear discharge .
Clinical diagnosis of organism present .
Film .
Culture . .

Notes of "Angular Conjunctivitis" were not recorded until July 1, 1905. Certain cases of conjunctivitis were not included in the series, namely, those obviously due to injury and those in which lachrymal obstruction occurred. A difficulty presented itself as regards cases in which phlyctenules were present. Those only were included in which the conjunctival congestion was not limited to the neighbourhood of the phlyctenule.

The micro-organisms which we attempted to clinically forecast as being present in the conjunctival sac, were Koch-Week's bacillus, the diplobacillus of Morax and Axenfeld, the gonococcus, the tubercle bacillus and the diphtheria bacillus. When it was believed that none of these forms could be demonstrated by a bacteriological examination, a diagnosis of "other forms" was made. This term is employed for the sake of brevity throughout this article.

Technique Employed in the Consecutive Series Examined in 1905.

It was originally intended to take two films and one culture from each case, one film to be stained in the usual manner by Löeffler's methylene blue. Should a doubt arise as to the presence of certain organisms, the other film would be stained by the method of Gram. The scarcity of discharge in many of the cases rendered this triple procedure impossible, and at times it had to be decided whether to take a single film or only a culture. Hence, as a routine practice, a single film and a culture were taken.

Films.—The material from the conjunctival sac was removed by means of a sterilised platinum wire and smeared over a glass slide. It was dried by exposure to the air, fixed by heat, stained by means of Löeffler's methylene blue, and examined microscopically.

Cultures.—During the preliminary observations 2-per-cent. agar was employed and the body fluids were added in the proportion of one to three. Later the amount of fluid added was increased, but it was found that media so prepared were not sufficiently firm to retain a sufficiently level surface when exposed to the heat of the incubator. 2·5-per-cent. agar was thereafter employed, mixed with equal parts of the body fluids. This method was retained throughout the consecutive series. In all, nine body fluids were used for the cases in this series. Some of these were early abandoned, others proved so satisfactory that they were employed until they were exhausted. The striking difference in the relative value of various fluids led latterly to a rough investigation as to the amount of albumin in them, and to evidence of the presence of blood; the early fluids were not tested. The media and fluids employed in the inquiry are designated as follows:—

A. Ovarian fluid obtained in 1904.

B. Ovarian fluid obtained on March 11, 1905. This fluid tested by Esbach's albuminometer showed 7 per cent. of albumin present. A portion of the fluid heated with ammonia and ammonium sulphide gave the spectrum of hæmochromogen.

C. Ovarian fluid obtained on April 29, 1905 (not tested).

D. Ascitic fluid obtained on April 29, 1905, contained 4 per cent. of albumin and did not yield the hæmochromogen spectrum.

E. Parovarian fluid obtained on July 29, 1905, contained 0·15 per cent. of albumin; spectrum of hæmochromogen not obtained.

F. Ovarian fluid obtained on October 7, 1905, contained 7·5 per cent. of albumin; spectrum of hæmochromogen observed.

G. Ovarian fluid got on November 25, 1905, contained 5 per cent. of albumin; spectrum of hæmochromogen observed.

H. Ovarian fluid got on December 15, 1905, contained 5 per cent. of albumin; hæmochromogen present.

I. Hydrocele fluid got on September 7, 1905; 5½ per cent. of albumin and no hæmochromogen.

The number of conjunctivitis cases in the consecutive series examined during 1905 was 820. The total number of all eye cases was 3,527. Conjunctivitis, therefore, formed 23·24 per cent of the cases. In v. Michel's Jahresbericht, statistics, extending from 1885 to 1895, from various clinics in different countries, embracing 599,595 cases of eye disease, showed that the most frequent eye disease was that affecting the conjunctiva. It amounted to 28·5 per cent. Cohn, in a collection of 297,326 cases, found that conjunctival diseases were 30 per cent.

Koch-Week's Conjunctivitis.

There were 310 bacteriologically proved cases of this form in the series of 820 cases of conjunctivitis.

Out of the 820 cases there were selected :—

(1) All cases clinically diagnosed as due to Koch-Week's bacillus.

(2) All cases bacteriologically proved to have Koch-Week's bacillus present.

These were then grouped as follows :—

1. Cases clinically diagnosed as due to Koch-Week's bacillus and confirmed bacteriologically. There were 268 cases. Of these, 242 were clinically diagnosed as due to Koch-Week's bacillus and bacteriologically confirmed, hereafter referred to as Group A. Twenty-six cases, clinically diagnosed as due to Koch-Week's bacillus, were proved bacteriologically to have in association both Koch-Week's bacillus and the diplobacillus ; hereafter referred to as Group B.

2. Cases diagnosed clinically as due to Koch-Week's bacillus but not confirmed as such bacteriologically. In this group were 78 cases, hereafter referred to as Group C.

3. Cases wrongly diagnosed—30 as "other forms," 12 as diplobacillus—which were shown bacteriologically to be due to Koch-Week's bacillus. In this group were 42 cases, hereafter referred to as Group D.

In all, 388 cases were thus analysed. As far as possible the age, history and objective signs of the cases in each of these groups are given in tabular form. The various items noted in the schedules are given seriatim.

Age Incidence.

Age.	Group.				
	A.	B.	C.	D.	A + D.
Under 1 year ...	17	1	3	4	21
1—4 years	53	8	10	3	56
5—13 years	144	13	40	14	158
Above 13 years ...	28	4	25	21	49
Total cases ...	242	26	78	42	284

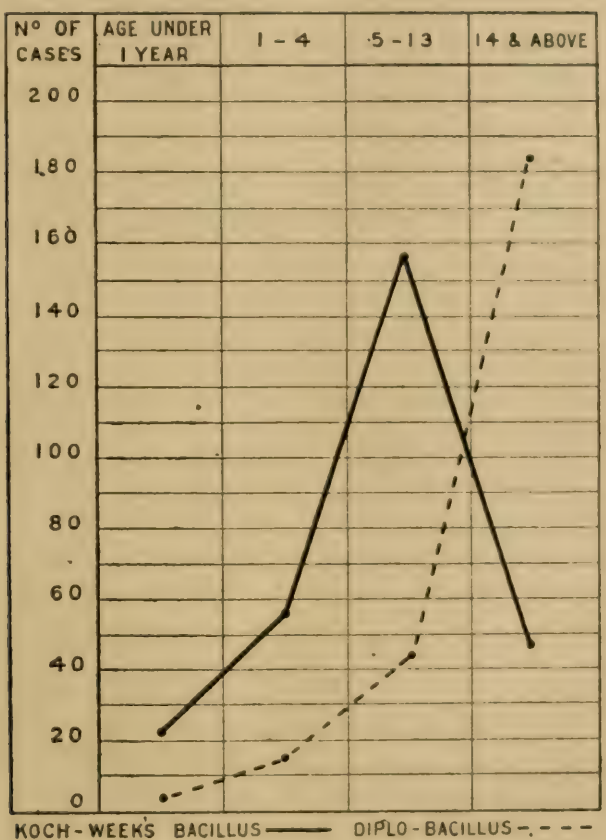


Table to show, at different age periods, the relative prevalence of conjunctivitis, proved bacteriologically to be due to—

(1) Koch-Week's bacillus } (exclusive of the cases in which both these
(2) Diplobacillus } organisms were found associated.)

Interval since Onset of the Attack.

In Group A (242 cases), presumably the more typical cases, it was found that the average length of the period during which symptoms had been present was 6·8 days. In 42 the interval was not more than 2 days. In 77 there was an interval of from 3 to 4 days. Sixty-seven patients came for treatment at the end of 7 days; 25 on the 14th day, and only 10 came after a longer period, of whom 5 came at 21 days; one, an infant of ten months, was said to have had symptoms of conjunctivitis for four months. In Group B (26 cases) 25 came for treatment on an average after an interval of 5·9 days, 3 of these after symptoms had been present for 14 days; all the others came within one week. The 26th case, the only one clinically diagnosed as containing both Koch-Week's bacillus and the diplobacillus, came after an interval of 21 days. Of 30 cases under Group D recorded clinically as due to "other forms," but which were shown to contain Koch-Week's bacillus, 24 came within a week. One said that symptoms had been present for one year, and another for two years. The remainder came at intervals varying from 14 days to three months. The suggested explanation of the long duration of the symptoms in some of these cases is that the diplobacillus was present as well as Koch-Week's bacillus, and in all likelihood was responsible for symptoms prior to the more recent infection by Koch-Week's bacillus. In Group C (78 cases) 58 came after an interval of not longer than one week.

An attempt was made to determine the duration of this form of conjunctivitis by consulting the case papers. These showed that the vast majority of the cases did not return. The same is true for the diplobacillary cases.

Previous Attacks.

In Group A were 25 cases: 20 of these were under 14 years of age; one, a child of 11 months, was said to have

attended hospital for three months after birth on account of eye disease. We are aware that the previous attacks may have been due to other conditions, as seems likely in the 11 months' child just noted, but that a second attack of Kock-Week's conjunctivitis may occur in the same individual, was proved in the case of two boys. The bacillus was obtained in each case during an attack of conjunctivitis in 1904, and again during a second attack about 18 months later, in 1906.

Group B, no cases. This might favour the view that Koch-Week's bacillus was the primary cause of the infection; recurrences are less common in cases due to the Koch-Week's bacillus than in those due to the diplo-bacillus.

Group C, 17 cases. Five of these would still be regarded as due to Koch-Week's conjunctivitis (*vide infra*).

Group D, 8 cases.

There was, therefore, a history of previous attacks in 33 of 310 cases of Koch-Week's conjunctivitis.

Others Affected with the same Symptoms.

	Group.				
	A.	B.	C.	D.	A + D.
In same house ...	131	16	35	15	146
Elsewhere	58	5	10	3	61

Certain cases gave a history of others affected both in the same house and elsewhere.

In Group A, in 167 cases, there is a history of other persons being affected with similar symptoms. In 131 instances others that were affected lived with either the patient's family or with other families in the same tenement.

In 58 instances other affected persons did not live in the

same house, but some attended the same school. Three-fourths of the cases in this group came as patients to the dispensary, where, generally speaking, a poorer class is seen than at the hospital. Their conditions and habits would favour the spread of an infectious disease.

Group B. In 19 cases it was reported that there were persons affected similarly; in 16 instances the affection being in the same house, in 5 instances elsewhere.

Group C. In 40 cases other individuals were known to be affected; in 35 the affection was in the same house as our patient, in 10 instances it was elsewhere.

As evidence of the infectious nature of Koch-Week's conjunctivitis, may be mentioned the occurrence of several small epidemics which came under our notice during the course of this investigation. In one of these an outbreak occurred in a certain street from which a number of typical Koch-Week's cases were obtained. Three of the cases were members of the same family, others were from adjoining houses. Seven of the cases, representing five different families, from three adjoining tenement houses, were examined. All were Koch-Week's cases. In September 1904, an opportunity arose for investigating an outbreak occurring in an industrial school in Aberdeen. At this institution there are about 130 boys, aged from five to sixteen. At the time of our first visit 12 boys were affected with Koch-Week's conjunctivitis, their ages varying from eight to fourteen years. The specific micro-organism was obtained in each case. Two other boys with the same form of conjunctivitis were examined later. Some cases had occurred previous to our visit. At the end of May, 1904, the first case was observed. On June 20 there were three more, by June 23 four others occurred; by the 30th four more were added, by July 12 there were six new cases. In August, seven new cases occurred. In September nine new cases, 34 in all, or about one-fourth of the inmates in the institution, had been affected. The children used towels in common. The individuals affected were isolated until cured. Notwith-

standing that the condition as regards use of towels, etc., had not been altered, no further case had been reported from September, 1904, until January, 1906. On January 30, 1906, six boys were affected. The attack was mild in each case. There were none with conjunctival hæmorrhages. The Koch-Week's bacillus was found in every case. Three of them had been previously affected in 1904, and at that time in two of these we had found the Koch-Week's bacillus. Recurrences at short intervals have been noted by Morax and Petit and also by L. Müller.* The latter observer described one case in which the interval was several months. Previous epidemics have occurred at this institution, but there is no record of any bacteriological examination.

(1) In May, 1894, 13 boys were affected with ophthalmia.

(2) May and June, 1897, 17 were affected with ophthalmia.

(3) October, 1899, to May, 1900, from 70 to 80 boys were affected.

As regards the relative frequency of Koch-Week's conjunctivitis in town and country, see p. 488. None of the cases in this series came from rural districts.

* Quoted from Kolle u. Wassermann.

Increased Redness of Conjunctiva.

	Group.				
	A.	B.	C.	D.	A + D.
Ocular and palpebral ...	225	22	67	30	255
Palpebral only	17*	4†	11‡	12§	29
Total cases ...	242	26	78	42	284

Of the 310 cases in which Kock-Week's bacillus was shown to be present, 33 had only the palpebral conjunctiva affected. One-third of these (11 in 33) occurred in infants. A moderate amount of discharge was present in three of the 11 cases; in the remaining eight, this was scanty.

Amount of Conjunctival Discharge.

	Group.				
	A.	B.	C.	D.	A + D.
Scanty	65	8	47	29	94
Moderate	158	18	29	13	171
Profuse	19	0	2	0	19
Total cases ...	242	26	78	42	284

* The interval since onset of symptoms in six of these did not exceed seven days, in two it was 14 days, in one it was 21, and in another it was 30 days. Seven occurred during infancy; one of these was said to have had symptoms of conjunctivitis present for four months.

† Of these, one was an infant with symptoms present for one day. Two were in children of three and four years, with symptoms present for seven and 14 days respectively. One was in a woman of 35, with symptoms for eight days.

‡ Ten of these came after symptoms had been present for a week or less, and one after 14 days. In no case was the age less than three or over 25 years.

§ Of these 12, three were in infants. One was in a patient aged 74, Case 421, in which both the diplobacillus and Koch-Week's bacillus were found; one in a patient aged 49, and another was aged 34. In none of the remaining cases did the age exceed 24.

Did the small amount of discharge occur in cases which came at an early or at a late stage of the disease? Of the 65 cases with scanty discharge, in Group A, 43 came within four days of the onset of symptoms, 10 on the 14th day, or later. Of the 29 cases with scanty discharge in Group D, 10 came within four days of the onset of the symptoms, 13 on the 14th day, or later. This gives 94 cases of proved Week's conjunctivitis with scanty discharge, of which 53 occurred within four days of the onset of symptoms, and 23 on the 14th day, or later, *i.e.*, 76 cases occurred within four days or later than 13 days, *i.e.*, 80·85 per cent.

Of the 158 cases with a moderate amount of discharge, in Group A, 70 came within four days of the onset of symptoms; 23 on the 14th day or later. Of the 13 cases with a moderate quantity of discharge, in Group D, 7 came on the 4th day or earlier, 5 on the 14th day or later. On adding together the cases with moderate discharge, in Groups A and D, there are 171 cases of proved Koch-Week's conjunctivitis, of which 77 came within four days of the onset of symptoms and 28 on the 14th day or later, *i.e.*, 105 occurred within four days or later than 13 days, *i.e.*, 61·40 per cent.

Of the 19 cases with profuse discharge in Group A, in 10 symptoms had been present for four days or less, and in two for two weeks or longer.

In Group B, of the eight cases with scanty discharge, two had had symptoms for four days, and in two symptoms had been present for 14 days. Of the 18 cases with moderate discharge, in nine symptoms had been present for four days or less, and in three cases for 14 days.

In Group C, of the 47 cases with scanty discharge, 20 came at an interval not exceeding four days after the onset of the symptoms; six at an interval of two weeks or longer. Of the 29 cases with moderate discharge, six came after an interval of four or fewer days, and 11 cases after 14 days. One with profuse discharge came on the 3rd day, the other on the 7th day.

The Discharge was almost invariably of a muco-purulent character and requires no further comment.

Presence of Enlarged Conjunctival Follicles.

Group A—35,* B—6, C—9, D—8.†

Presence of Conjunctival Hæmorrhage.

Group A—57, B—3, C—13, D—1.

Chemosis.

In Group A chemosis is noted twice; in none of the other three groups was it met with.

Membrane on the conjunctiva was present in four of the cases in Group A.

Presence of Swelling of Lids.

Group A—210, B—22, C—63, D—23.

Presence of Enlarged Preauricular Gland.

Group A—84, B—7, C—32, D—6.

In infants an enlarged preauricular gland has not been observed.

Proportion of Uniocular to Symmetrical Cases.

	Group.			
	A.	B.	C.	D.
Uniocular	21‡	1§	15‖	10¶
Symmetrical...	221	25	63	32

* Thirty-one were in children. † Seven were in children.

‡ Only three of these presented themselves for examination later than the 4th day after the onset of symptoms, one on the 5th day, and two on the 7th day.

§ Symptoms had been present for only one day.

‖ Of these, six came after the 4th day from the onset of the symptoms, one on the 5th day, and five on the 7th day.

¶ In three of these, symptoms had been present for longer than four days. One, a child of seven, had complained for 21 days; another case, aged 34, had symptoms for 30 days; and the third case, a child of three months, for 90 days.

Presence of Corneal Ulcers, etc.

	Group.			
	A.	B.	C.	D.
Corneal ulcers	1	0	2	2
Impetigo	3	1	1	1
Phlyctenules	35	3	6	2
Nasal discharge	16	1	2	0
Aural discharge	1	0	0	0

Phlyctenules were noted in 53 of the 820 cases of conjunctivitis in the series. In 36 of these the staphylococcus was present. In five of the 53 cases Koch-Week's bacillus only was found; in 31 of the 53 cases Koch-Week's bacillus was found in association with one or more of the following micro-organisms: staphylococcus pyogenes aureus and albus, xerosis bacillus and streptococcus pyogenes.

In four of the 53 cases Koch-Week's bacillus and diplobacillus were found together. In two of the 53 cases diplobacilli only were found. In one diplobacillus associated with staphylococcus pyogenes albus and xerosis bacillus. In nine staphylococcus pyogenes aureus and albus or xerosis bacillus, one or more, were found. In one, pneumococcus was found with staphylococcus pyogenes albus.

Clinical Diagnosis.

Subjective symptoms are of but little assistance in distinguishing Koch-Week's conjunctivitis from that caused by other micro-organisms. In three-fourths of the 820 cases of conjunctivitis examined, the complaint made was of a gritty or similar feeling in the eyes, or of gumminess of the lids in the morning. Usually both of these symptoms were present. In the 310 cases where Koch-Week's bacillus has been proved to be present, only 28 times was any other

complaint made, such as difficulty in reading, the appearance of rainbows, etc.

The schedules of the 78 cases in which Koch-Week s bacillus was diagnosed but not found, have been reconsidered, since the facts brought out in the series of 820 cases have been tabulated, and there is reason to believe, from their clinical features, that thirty-two of them were caused by Koch-Week's bacillus, which organism was not obtained because—

(1) The amount of discharge was scanty.

(2) A film only may have been taken.

(3) A culture only may have been taken. When a film and culture are both taken, our experience has shown us that the organism may be absent in one and yet present in the other. It may be that the available discharge was used up for the first specimen, but we are unable to state whether the positive preparation was taken first.

(4) The culture media may have been unsatisfactory.

(5) The interval between the inoculation of the medium with the conjunctival discharge and the placing of the same in the incubator may have been too long. Unavoidable delay sometimes occurred. Squares of linen (5 mm.) soaked in the discharge, placed in sterilised Petri's dishes and exposed to room temperature, yielded cultures of Koch-Week's bacillus after two hours, but not after four. Weichselbaum* and Müller found that particles of secretion placed in a dried Petri dish did not yield cultures after $6\frac{1}{2}$ hours. Hofmann† found after exposing the discharge for three hours in dry Petri's dishes that the bacilli died.

In eight cases in which the pneumococcus was demonstrated, there were no clinical characters which would serve to differentiate them from a conjunctivitis caused by the Koch-Week's bacillus. In ten cases a clinical diagnosis would be a mere hazard. Twenty-five cases should now have

* Archiv f. Ophthalmologie, vol. xlvii, 1899, S. 108, quoted from Kolle u. Wassermann (Handbuch der pathogenen Mikro-org.).

† Zeitschrift f. Hygiene, vol. xxxiii, 1900, S. 109, quoted from Kolle u. Wassermann (Handbuch der pathogenen Mikro-org.).

been diagnosed differently; thus in case No. 3 a patient, age 73, the age alone makes the presence of Koch-Week's bacillus most unlikely, as, in the series, no case of conjunctivitis due to this bacillus has been met with in patients over 50 years of age, with the exception of a single case in which it was present with the diplobacillus. For the same reason Case 53, a patient aged 64, and Case 57, a patient aged 67, would not likely be due to Koch-Week's bacillus.

In the next three examples the history of *previous attacks* would favour the view that the micro-organism present was the diplobacillus.

Case 45, a child of six years, whose conjunctivitis was due to the diplobacillus, is one that would be difficult to distinguish from a Koch-Week's conjunctivitis. One week after the onset of symptoms there was a moderate amount of muco-purulent discharge, both palpebral and ocular conjunctivæ were congested and the lids swollen—signs which, in conjunction with the age, are suggestive of Koch-Week's conjunctivitis. On the other hand, the history of previous attacks would rather favour the view that the conjunctivitis was due to the diplobacillus.

Case 127 should have been recognised as due to the diplobacillus. A male, aged 13, interval since onset of symptoms five days, previous attacks, ocular conjunctiva not congested, scanty discharge, lids swollen and both eyes affected.

Similarly, Case 196, a female, aged 8, interval since onset of symptoms one week, previous attacks, others affected elsewhere, palpebral conjunctiva congested, but the ocular conjunctiva unaffected, moderate amount of muco-purulent discharge, lids swollen and both eyes affected. The diplobacillus was found.

Significance of the Uniocular Character of Conjunctivitis.

Case 134 has but one point which would throw doubt on a diagnosis of the Koch-Week's bacillus, namely, that after one week the affection was still uniocular. In 274 cases of proved Koch-Week's conjunctivitis 32 were uniocular; of these, 26 had had symptoms present for a period of not longer than four days.

Case 134, a female, aged 4, interval since onset of symptoms one week; others affected in the same house; both ocular and palpebral conjunctiva congested; moderate amount of muco-purulent discharge; conjunctival hæmorrhages; lids swollen, and one eye only affected. Film: cocci. Culture: staph. alb.

Cases of Koch-Week's conjunctivitis with only the palpebral conjunctiva affected (33 cases) may present difficulty in diagnosis.

Case 731, a male, aged one, brought after 14 days with the ocular conjunctiva unaffected, a moderate amount of muco-purulent discharge and both lids swollen; was diagnosed as a case of "other forms," but Koch-Week's bacillus was found present.

Cases to illustrate how an accurate diagnosis is impossible when the symptoms are obscured by treatment.

Case 212, a female, aged 27, who came after an interval of 4 weeks, with palpebral and ocular conjunctiva congested and a moderate amount of muco-purulent discharge, enlarged follicles; conjunctival hæmorrhages and both eyes affected. She had been using "golden ointment." In this case Koch-Week's bacillus was diagnosed, but staphylococcus pyogenes albus only was found.

Case 734, a male, aged 30, who had been using yellow ointment. Koch-Week's bacillus was found in the culture. Symptoms had been present for two days. Gumminess of lids; previous attacks; others affected; scanty discharge; swelling of lids; symmetrical. Clinical diagnosis: "other forms."

Conjunctivitis in a child where both palpebral and ocular conjunctiva is congested, the discharge is scanty, and no characteristic symptoms of either Koch-Week's or diplobacillary conjunctivitis are present may be due either to the diplobacillus or to Koch-Week's bacillus. Thus—

Case 23, a child aged 10, with palpebral and ocular conjunctiva congested, scanty discharge and no hæmorrhages or

other characteristic symptoms, diagnosed as Koch-Week's conjunctivitis, proved to be so.

Case 596, a child of 12, with similar symptoms, diagnosed as a case of Koch-Week's conjunctivitis; the diplobacillus was found in film and culture.

The two following cases are given as examples in which Koch-Week's bacillus may have been overlooked.

Case 717, a male child, aged 12, who came after an interval of three days with a history of others being affected in the same house, palpebral and ocular conjunctiva congested, discharge very scanty, lids swollen, and only one eye affected. Cases of conjunctivitis in children (palpebral and ocular conjunctiva congested) with only scanty discharge and where no pathogenic organism is found, are more likely to be due to Koch-Week's bacillus than to the diplobacillus, because (1) Koch-Week's bacillus is more common at this age than the diplobacillus. (2) Koch-Week's bacillus is more easily overlooked.

Case 128, a female, aged 17, who came after an interval of five days with palpebral and ocular conjunctiva congested, a moderate amount of muco-purulent discharge, lids swollen, and both eyes affected; is probably one in which Koch-Week's bacillus was overlooked. The diagnosis was Koch-Week's bacillus; film showed diplobacillus; no organisms were found in the culture; the medium was not satisfactory, and it is quite likely that when the conspicuous diplobacillus was found in the film the search was discontinued. In the 820 cases the Koch-Week's bacillus was shown to be associated with the diplobacillus 36 times. Axenfeld states that this mixed infection, according to general experience, is infrequent.

Of the 32 cases diagnosed as due to "other forms" and bacteriologically proved to contain Koch-Week's bacillus, the same diagnosis would still be made in 18 of them. In 12 a different diagnosis would be given, and in two a diagnosis would only be a guess.

The next four cases were all believed at the clinical examination to have been caused by Koch-Week's bacillus, but for reasons assigned it seemed unlikely that the bacillus

could be demonstrated; in consequence "other forms" were diagnosed.

Case 70, a male, aged two, with symptoms for two weeks, was complicated by the use of yellow ointment. Diagnosis, "other forms." Film and culture—Koch-Week's bacillus.

Case 13, a child, aged 11 weeks, with symptoms present for one day; discharge scanty; others affected elsewhere; previous attacks; uniocular; illustrates what we have from time to time met with, namely, cases which we felt were caused by Koch-Week's bacillus, but where, owing to the scanty discharge and the short duration of symptoms, it was thought unlikely that the bacillus would be obtained, hence the diagnosis of "other forms" in this instance. Koch-Week's bacillus was present.

Case 77, a female, aged 5, also had slight symptoms. Koch-Week's bacillus was found in the film, but not in the culture, which illustrates also the importance of taking both a film and a culture.

Case 730, which was one in which Koch-Week's bacillus was found in the culture but not in the film.

Cases which illustrate the unreliability of history in some instances.

Case 199, a child aged three months, in whom symptoms were said to have been present since birth.

Case 282, a child aged six years, where symptoms had been present for two months. In both of these Koch-Week's bacillus was present.

Case 644, a female age 13, with symptoms said to have been present for longer than a year, a history of previous attacks, no others affected, ocular conjunctiva not congested, scanty muco-purulent discharge, lids swollen and both eyes affected. Koch-Week's bacillus was found.

It is improbable that the symptoms in these cases caused by a conjunctivitis due to Koch-Week's bacillus had lasted for such a long period; for of the 274 proved cases of Koch-Week's conjunctivitis, only six in all gave a longer history than one month.

The clinical diagnosis of Koch-Week's conjunctivitis cannot be based upon one or two symptoms alone, but must depend upon a consideration of several features, namely, the age, history—previous attacks, interval since onset of attack, etc.—and objective symptoms. In a considerable proportion of the cases no doubt can attach itself to the diagnosis, as in these three typical examples :—

Case 700, female, aged 12, living in town, sore eyes and lids gummed in the morning for three days ; no previous attack ; others affected in the same house ; palpebral and ocular conjunctiva congested ; moderate quantity of muco-purulent discharge ; enlarged follicles ; conjunctival hæmorrhages ; swelling of lids ; preauricular gland enlarged ; symmetrical. Diagnosis : Koch-Week's bacillus. Film and culture gave Koch-Week's bacillus.

Case 445, a male, aged six, living in town, with sore eyes and gumminess of lids for three days ; no previous attack ; others affected in the same house and elsewhere ; palpebral and ocular conjunctiva affected ; moderate quantity of muco-purulent discharge ; conjunctival hæmorrhages ; swelling of lids ; preauricular gland enlarged ; symmetrical ; phlyctenules. Diagnosis : Koch-Week's bacillus. Film and culture showed Koch-Week's bacillus.

Case 704, a female, aged seven, living in town, with sore eyes and gumminess of lids for seven days ; no previous attacks ; others affected in the same house ; palpebral and ocular conjunctiva affected ; moderate quantity of muco-purulent discharge ; conjunctival hæmorrhages ; swelling of lids ; symmetrical. Diagnosis : Koch-Week's conjunctivitis. Film and culture gave Koch-Week's bacillus.

In support of this it may be mentioned that towards the latter part of the series 35 of the cases presenting typical characteristics of Koch-Week's conjunctivitis were marked as "certain," and in every instance Koch-Week's bacillus was bacteriologically proved to be present. When all cases of Koch-Week's conjunctivitis are considered, there remain a large number in which the conditions are not perfectly

typical, but in which a correct diagnosis may usually be made by attention to the presence of several of the more important characteristics. (1) The age—the fact that so many of the cases occurred at the school period is important. (2) A short interval since onset of symptoms, such as from three or four to seven days. (3) A history of others being affected with similar symptoms. (4) The involvement of the ocular conjunctiva. (5) Muco-purulent discharge in fair amount. (6) The presence of conjunctival hæmorrhages. Conjunctival hæmorrhages occurred in 21·16 per cent. of the proved Koch-Week's cases; in 0·86 per cent. of the proved diplobacillary cases and in 8·8 per cent. of all other cases in which these organisms were not found. (7) Cases coming from rural districts are unlikely to be Koch-Week's cases, since in this series we have not met with one such case. It is mainly in the differential diagnosis between Koch-Week's conjunctivitis and the diplobacillary form that difficulties have arisen.

In the series of 820 cases of conjunctivitis a clinical diagnosis of the presence of Koch-Week's bacillus was made in 346 cases, and confirmed in 268 or 77·4 per cent. If the 32 cases which are still considered to have been due to this bacillus are included (*vide* p. 450), there are then 300 cases, *i.e.*, 87 per cent., in which we believe the clinical diagnosis was correct. Calculating from the number of times Koch-Week's bacillus was met with in the series, and the number of times a clinical diagnosis of this organism was made, we find that, out of 310 cases bacteriologically proved to contain Koch-Week's bacillus, a correct clinical diagnosis was made 268 times, *i.e.*, in 86·4 per cent. of cases.

Films.—These, made directly from the secretion of the conjunctival sac, were stained in a manner previously mentioned. Koch-Week's bacilli by this method are seen as fine rods about 0·5 μ to 1 μ in length, occasionally somewhat longer. At times two are joined end to end. Their ends appear somewhat rounded, frequently they are met with intracellularly. The cells of the secretion are some-

times seen to contain a number of these bacilli. There is nothing characteristic in this arrangement, for the bacilli are met with just as frequently extracellularly. In films where the bacilli are scanty a prolonged search may be necessary, and if bacillus xerosis is present, a doubt might arise whether the one or two slender rods met with are really Koch-Week's bacilli. It is here that the importance of staining the film by Gram's method becomes evident. It was our original intention to take two films from each case, one of which was to be treated by Gram's method with contrast staining by means of safranin. We found, however, that the amount of discharge in those cases in which a doubt was likely to arise was not sufficient to give two films as well as a culture.

Cultures.—The discharge for the culture was as far as possible taken from the conjunctival sac and not from that which had collected at the inner canthus. The former material was less likely to be contaminated with saprophytic organisms than the latter. The tubes, when inoculated, were transferred to the incubator with the least possible delay; at times, however, the interval elapsing before doing so has been an hour or two, and this we believe to be disadvantageous from the point of view of successful cultivation. These tubes were examined after at least 48 hours' incubation. Colonies of the Koch-Week's bacillus were visible, and presented an extremely minute dew-drop character, which was rendered more evident by examination with a low magnifiying power and resembled those described by Axenfeld.* When associated with the presence of one or two staphylococcus colonies these dew-drops were more conspicuous. With bacillus xerosis, whose colonies are much smaller than those of the staphylococcus, the prominence given to the Koch-Week's colonies was not so marked. In pure cultures, which have been obtained from time to time directly from the conjunctival discharge, Koch-Week's

* Handbuch der pathogenen Mikro-organismen, Kolle u. Wassermann, 1905.

colonies, although occasionally abundant, had to be carefully looked for. This prominence of Koch-Week's colonies in the neighbourhood of staphylococcus and xerosis colonies, so well marked in the case of the former, would lend support to the symbiotic view which has been put forward. In association with colonies of diplobacilli, colonies of Koch-Week's bacilli are not so conspicuous as when associated with either of the two former organisms, perhaps due to the greater contrast between the white and yellow colonies of the two former organisms as contrasted with the semi-transparent colonies of diplobacillus. Films were made from the cultures and stained by the Gram and safranine method already mentioned. Microscopically in such films the Koch-Week's bacilli were usually recognised without difficulty, the red stained slender rods contrasting with the larger red stained diplobacilli, the violet stained cocci or bacillus xerosis when present.

The *media* most suitable for the growth of this organism was ovarian agar. The ovarian fluid should be recently obtained. It was found that fluid containing from 5 to 7 per cent. of albumin, as tested by Esbach's albuminometer, also blood derivatives, the presence of which were proved by obtaining a spectrum of hæmochromogen, was most suitable for preparing the ovarian agar. After being kept for six months or thereby, ovarian fluid, although sterile, does not yield a satisfactory culture of Koch-Week's bacilli. When the series was begun, in 1905, the ovarian fluid employed was some six months old, and it was noted that the medium made was not furnishing satisfactory cultures of the bacilli. That the fluid was originally a good one cannot be doubted, for it was by the use of it in August and September of 1904 that Koch-Week's bacilli were isolated in pure culture and carried through 30 to 40 generations. It was suggested that light, since it exercises photo-chemical phenomena on certain fluids exposed to it, might have had a deteriorating influence on the fluid; it was therefore decided to keep the future fluids and prepared media in the dark. Fluid B (see

page 439), so stored, obtained on March 11, 1905, yielded successful cultures of Koch-Week's bacilli as late as October 11, that is seven months after it was obtained; it was then exhausted.

Other fluids which had been tried for the culture of Koch-Week's bacilli have in no instance been so successful as recently obtained brown viscid, ovarian fluid. Fluid E, a parovarian fluid, obtained on July 29, which contained no blood derivatives and only 0·15 per cent. of albumin, was quite unsatisfactory. Fluid D, an ascitic fluid from a case of tubercular ascitis, containing 4 per cent. of albumin and no blood derivatives, was so unreliable that its use had to be discontinued. Fluid J, a hydrocele fluid containing 5·5 per cent. of albumin and no blood derivatives, furnished fairly good cultures. Its use, however, was not continued, as for our requirements there was sufficient good ovarian fluid whose reliability could not be called in question. Blood-smeared agar was tried on several occasions. We have almost invariably failed to obtain cultures by this method, although the cases in which it was tried were those in which films of the discharge showed Koch-Week's bacilli. The agar was smeared with human blood taken from the finger, and also from the conjunctival vessels by the method suggested by Bishop Harman.* The latter procedure was, in our hands, unsatisfactory, inasmuch as it entailed needless discomfort to the patient and frightened children, in whom the majority of such cases occur.

Isolation of Koch-Week's Bacilli.—In September, 1904, during the epidemic of Koch-Week's conjunctivitis at the Industrial School before mentioned, cultures were taken from 12 cases. Eleven of the culture tubes showed colonies of the bacillus. Sub-cultures were made from each of these. Koch-Week's colonies were recognisable in most of the sub-cultures. In the remainder the saprophytic organisms had grown so profusely that isolation, by further sub-culture, would have been extremely difficult. It was

* The Conjunctiva in Health and Disease, p. 48.

decided to devote attention to those cultu
Koch-Week's colonies were relatively nume
pared with colonies of other organisms. Ev
a series of sub-cultures, this became narro
dealing only with sub-cultures obtained fron
cases. The organism was in this case growi
the diplobacillus. Successive streaks were ma
agar, and eventually Koch-Week's bacillus
in pure culture. Mixing the impure culture
fluid, in Petri's dishes, thereafter adding liqu
agar and incubating, failed as a means of is
colonies of Koch-Week's were either so small
or so mixed up with the diplobacillus, that
and recultivation was impossible. In the 24 ho
the Koch-Week's bacillus and diplobacillus on
the diplobacillus colonies were evident by their
semi-transparent appearance, whilst at inte
streaks were seen the minute, punctate, transp
of Koch-Week's bacilli. Similar cultures on
presented no appreciable difference. Pure cu
Koch-Week's bacillus were made on ovari
ascitic agar. They presented the same chara
media; after 48 hours they were punctate, a
nine days or longer in the incubator there was
increase in the size of the colonies. The colo
Week's bacillus when grown alone were no
different in size from those grown along wi
bacillus, although the presence of the diploba

the staphylococcus and other colonies. These were after incubated for 48 hours. On examination especially noticeable that the growth of Koch-bacillus was in every instance most luxuriant in pr to the streaks of the other organisms. It must, howe stated that the streaks of Koch-Week's bacilli adja the other organisms had in each instance been made the more distant ones. The colonies adjacent to streaks of other organisms were in no instance larg those more distant. The pure culture of Koch-bacillus was carried through nearly 40 generations later sub-cultures of Koch-Week's bacilli showed abu of involution forms (photo 2), which were lon threadlike, and in other instances formed quite a mass. In a 48 hours' culture, whilst these were abun a 96 hours' culture they predominated still more, an 10 days the thread forms were much broken up an was an abundance of granular débris.

When a pure culture of Koch-Week's bacill obtained directly from the conjunctival discharge i occurring in the series taken in 1905, attempts wer from time to time to obtain sub-cultures. These obtained, but they have shown a marked tendency to after the third or fourth generation. It is possible that symbiosis may be of value in aiding the growth Koch-Week's bacillus. When repeated sub-culture been made of the bacillus in association with an or such as the diplobacillus, it may have become so ada saprophytic conditions that when isolated therefr

dissolved in 20 c.c. of distilled water were placed. This was then sterilised, as also were a trochar and canula with long rubber tube attached to it. These were then taken to the slaughter-house; directly an ox was killed the skin and subjacent tissues were dissected up, the jugular vein exposed, and the canula inserted. The blood was then allowed to flow through the canula and tube. The first quantity being rejected, the flask was thereafter filled and replugged with the cotton wool. This citrated blood, which contained 0·25 per cent. of citrate of soda, was then mixed with nutrient agar in a manner similar to that already described for the preparation of ovarian agar. A rich red coloured medium was thus obtained. When Koch-Week's bacillus was streaked on such a medium the colonies were very readily visible to the naked eye, much more so than on any of the other media employed. As the ovarian agar, of which there was sufficient quantity, was quite satisfactory for the growth of Koch-Week's bacillus, and as it was thought that the citrated blood medium would be less reliable from the point of view of contamination, we did not continue to use it.

Out of 310 proved Koch-Week's cases a culture and a film were taken in 282. Both the culture and film showed the presence of the bacillus in 187 of them. In 82 of the 282 cases the film was positive and the culture negative. In 13 of the 282 cases the film was negative while the culture was positive. This gives a total of 200 cultures obtained. If the number of cultures in cases where no film was taken are included, we then find that the bacillus was obtained 232 times.

When the various media employed are compared and consideration given only to such cases as were proved by the film to contain Koch-Week's bacilli, it is found that of 39 inoculations of fluid A 16 were positive and 23 negative. The majority of the negative ones occurred when the fluid had been kept longer than six months. Of 55 inoculations on medium B 45 were positive and 10 were negative. This fluid was used only for a short time after it had been

obtained. On medium C of 58 inoculations 51 were positive, seven were negative. On medium D, of 14 inoculations five were positive and nine were negative: such a result led to the abandonment of this medium. On fluid E of 17 inoculations six were positive and 11 were negative. This medium was then also abandoned. On medium F there were three inoculations, and all were negative. On medium G there were 44 inoculations with 33 positive and 11 negative. On medium H there were 35 inoculations with 28 positive and seven negative. On medium I, which was obtained towards the conclusion of the series, there were four inoculations, three positive and one negative.

Diplobacillary Conjunctivitis.

There were 274 bacteriologically proved cases of this form in the series of 820 cases of conjunctivitis.

Out of the 820 cases there were selected (1) all cases clinically diagnosed as due to the diplobacillus; (2) all bacteriologically proved cases of diplobacillary conjunctivitis. These were then grouped as follows:—

(1) Cases clinically diagnosed as due to the diplobacillus and bacteriologically confirmed; of such there were 176 cases. Of these, 171 diagnosed as due to the diplobacillus and confirmed bacteriologically are hereafter referred to as Group A. Five diagnosed as due to the diplobacillus in which both Koch-Week's bacillus and the diplobacillus were present are hereafter referred to as Group B.

(2) Cases clinically diagnosed as due to the diplobacillus in which bacteriologically that organism was not demonstrated. There were 78 cases, hereafter referred to as Group C.

(3) Cases wrongly diagnosed, in which the diplobacillus was shown bacteriologically to be present. There were 67 cases, hereafter referred to as Group D; 31 were diagnosed as Koch's-Week's conjunctivitis, 36 as "other forms."

In all, 321 cases were thus investigated. This does not include (1) the 26 cases diagnosed as due to Koch-Week's bacillus and bacteriologically shown to contain both Koch-Week's bacillus and the diplobacillus already dealt with under Group B of the Koch-Week's series and (2) five cases in Group D of the same series.

Subjective Symptoms.

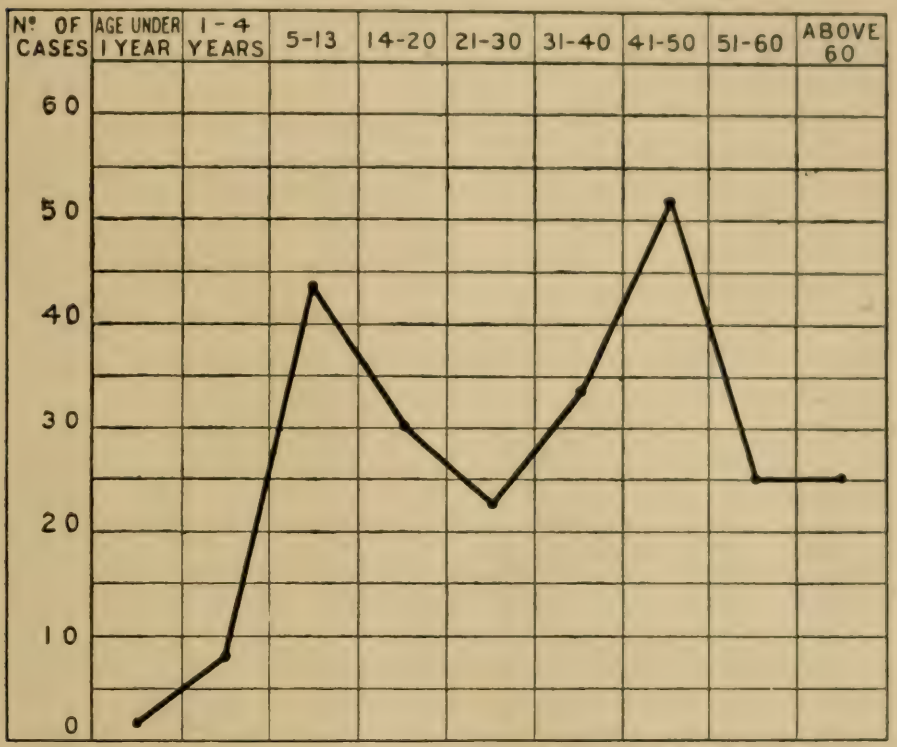
	Group.				
	A.	B.	C.	D.	A + D.
Grittiness, gumminess, or both ...	164	5	75	67	231
Difficulty in reading	15*	1	8†	1‡	16
Rainbows	1	1	1	0	1
Heavy lids	15	0	9	1	16
Other complaints	16	1	14	8	24

Age Incidence.

Age.	Group.				
	A.	B.	C.	D.	A + B + D.
Under 1 year	0	0	0	2	2
1—4 years	0	0	1	8	8
5—13 ,, ...	14	0	7	30	44
14—20 ,, ...	19	2	13	9	30
21—30 ,, ...	17	0	18	6	23
31—40 ,, ...	29	0	13	5	34
41—50 ,, ...	47	2	14	3	52
51—60 ,, ...	23	0	6	2	25
60 and upwards ...	22	1	6	2	25
Total cases ...	171	5	78	67	243

* Most of these were over 40 years of age.
† Six were under 40 years of age.
‡ Aged 12.

A table showing the number of proved diplobacillary cases at different age periods (it does not include 31 cases of diplobacillus, present with Koch-Week's bacillus, which were clinically diagnosed as Koch-Week's bacillus or "other forms") is shown graphically in the following chart:—



The number of cases under 14 years of age is 54. When those cases whose age was under 14 years are added from the 31 cases in which the Koch-Week's bacillus was associated with the diplobacillus (24), there are 78 cases in which the diplobacillus was found in children under 14 years of age.

Therefore children under 14 years of age were affected in 28·46 per cent. of the 274 cases in which the diplobacillus was demonstrated.

It is evident that the majority of cases of diplobacillary conjunctivitis occur in adults. There are, however, a considerable number to be met with in children, especially at the school period, and, in ignorance of this, a clinical diagnosis of this organism in children was seldom made,

especially during the first part of the inquiry. Of the 67 cases in Group D 40 occurred before the age of 14. Thus out of 54 cases of proved diplobacillary conjunctivitis in patients under 14 years of age only 14 were correctly diagnosed. Of the remaining 40, 31 were diagnosed as cases of Koch-Week's conjunctivitis. Out of 184 proved cases of diplobacillary conjunctivitis above the age of 13 years, 157 were correctly diagnosed.

Interval since Onset of Symptoms.

Interval.	Group.				
	A.	B.	C.	D.	A + D.
Under a week	30	1	18	40	70
14—21 days	51	1	23	13	64
28 days to 3 months ...	63	2	23	12	75
Longer	24	1	14	1	25

(Cases occurring between one week and 14 days, also between 21 and 28 days, are intentionally omitted.)

On comparing Groups A and D it will be seen that whereas in Group A with 171 cases 30 came within a week of the onset of symptoms, in Group D with only 67 cases there were 40 which came at a corresponding period. It should be noted in Group A that of the 30 cases which came not later that one week after onset of symptoms, 27 were adults, and three children. On the other hand, in Group D, of the 40 cases which came not later than one week after onset of symptoms, 30 were children and 10 adults.

When Groups A and D are combined it will be seen that of 238 cases of diplobacillary conjunctivitis 70 came within a week of onset of symptoms, 37 adults, 33 children. Of the 238 cases, without reference to onset of attack, 54 occurred in children, 184 in adults. It is, then, apparent that the interval between commencement of symptoms and the time when advice is sought is shorter in the case of children than it is in adults.

Previous Attacks.

A—48, B—0, C—30, D—21.

In Groups A and D, which together amount to 248 cases of proved diplobacillary conjunctivitis, 69 had previous attacks. (In Koch-Week's cases this was true of 33 in 284 cases.) On February 28, 1906, diplobacilli were present in a film taken from the discharge of an individual in whom this organism had been found on July 21, 1905.

Others Affected with the same Symptoms.

	Group.				
	A.	B.	C.	D.	A + D.
In same house	35	4	11	21	56
Elsewhere	5	0	4	8	13

Increased Redness of Conjunctiva.

	Group.				
	A.	B.	C.	D.	A + D.
Ocular and palpebral ...	72	2	37	51	123
Palpebral alone	99	3	41	16	15

Amount of Conjunctival Discharge.

	Group.				
	A.	B.	C.	D.	A + D.
Scanty	139	1	66	50	189
Moderate	32	4	12	16	48
Profuse	0	0	0	1	1

Character of Discharge.—The discharge, as in cases of Koch-Week's conjunctivitis, was of the usual muco-purulent character.

Presence of Enlarged Conjunctival Follicles.

Group A—16, B—0, C—5, D—12.

Presence of Conjunctival Hæmorrhage.

Group A—1, B—0, C—2, D—1.

The ages of these cases were respectively 41, 34 and 51, 41.

Presence of Swelling of Lids.

Group A—97, B—3, C—37, D—52.

Neither *Chemosis* nor *membrane* was present in a single case of any of the groups.

Presence of Enlarged Preauricular Gland.

Group A—22, B—1, C—3, D—20.

Angular Conjunctivitis was considered to be present when in association with a conjunctivitis there occurred increased redness of the edge of the lid, limited to its outer or inner end, or when in addition there was increased redness of the skin at either the outer or inner canthus. This condition was noted, when present, in every case from July 1 to December 31, 1905. Four hundred and forty-two cases of conjunctivitis were examined during that period, 121 of these were diplobacillary cases. In 42 of the 442 cases of conjunctivitis angular conjunctivitis was noted; in 37 of these the diplobacillus was found, *i.e.*, in 34·7 per cent. of the diplobacillary cases.

The remaining five cases are:—

Case 339 (exophthalmic goitre), with signs present at the inner canthus, a film and culture yielded only xerosis bacillus and staphylococcus pyogenes aureus and albus; the medium was satisfactory.

Case 455 had this symptom present at both inner and outer canthi, and in a film xerosis bacillus was found, and in culture staphylococcus pyogenes aureus and albus, the medium was unsatisfactory.

Case 652 had the outer canthus affected, no film was taken, culture yielded staphylococcus pyogenes aureus and albus; the medium was good.

Case 740 had the inner canthus affected, no culture. Two films were taken, but no organism was found in them.

Case 794 had signs at the inner canthus; Koch-Week's bacillus was found in the film along with staphylococcus pyogenes aureus and albus in the culture; medium good. It may be noted that in cases 740 and 455 there is a possibility of the diplobacillus having been missed, but as regards the other three cases this is not likely.

In 16 of the 37 cases with angular conjunctivitis occurring in diplobacillary cases the characteristic appearance was present both at the inner and outer canthus. In 18 cases it occurred at the inner canthus, the outer being unaffected. In three cases it occurred at the outer canthus, the inner being unaffected.

Though not systematically noted, it was remarked that several of these cases complained of itching at the outer and inner canthus, causing them to rub these situations.

Conclusions.

(1) Angular conjunctivitis occurs in about one-third of all conjunctivitis cases due to the diplobacillus.

(2) When angular conjunctivitis is present it is almost pathognomonic of the presence of the diplobacillus. In 88 per cent. of our cases of angular conjunctivitis this micro-organism was found.

Proportion of Uniocular to Symmetrical Cases.

	Group.				
	A.	B.	C.	D.	A + D.
Uniocular	8	0	4	17	25
Symmetrical	163	5	74	50	213

Presence of Corneal Ulcers, etc.

	Group.			
	A.	B.	C.	D.
Corneal ulcers	3	0	3	3
Impetigo	0	0	0	2
Phlyctenules	0	0	0	4
Nasal and aural discharge ...	0	0	0	0

Clinical Diagnosis.—In the clinical diagnosis of diplobacillary conjunctivitis, as in the case of Koch-Week's conjunctivitis, subjective symptoms are of but little value as a means of distinguishing the micro-organism. Either grittiness or gumminess of the lids or both are complained of in nearly every case. It may be mentioned, however, that of 238 proved cases of diplobacillary conjunctivitis, 16 complained of heaviness of the lids, and of the cases which were clinically diagnosed as due to the diplobacillus, though not bacteriologically confirmed, nine made the same complaint. In seven of these we should yet make a similar clinical diagnosis. There are possibilities of the micro-organisms having been overlooked for various reasons previously given under Koch-Week's conjunctivitis. As illustrating the slightness of the subjective symptoms, cases have been met with in which the patient came on account

of some condition other than conjunctivitis, *e.g.*, Case 544, which came on account of corneal injury, and Case 357, which came on account of advanced cataract. Again, in one member of a family who had had no subjective symptoms for some time, and in whom there were no objective signs of conjunctivitis, diplobacilli were obtained from the conjunctival sac. She was examined because her three sisters and mother, living in the same house, had unmistakable signs of conjunctivitis, and in each of them the diplobacillus was found. This case is not one of the series. Diagnosis must therefore rest mainly upon a grouping of age, history—previous attacks, interval since onset of attack, etc.—and objective symptoms.

Age.—Too much stress must not be laid on the age. In 171 cases clinically diagnosed and bacteriologically proved to be due to the diplobacillus, 99 occurred between the ages of 31 and 60. If we add those over 60 years of age, there is a total of 121. On the other hand, in those cases (67) wrongly diagnosed but bacteriologically proved to be due to the diplobacillus, 40 were under the age of 14. If these two groups be combined it is found that of 238 cases of diplobacillary conjunctivitis, 54 were under 14 years of age and 133 over 30; this indicates how important it is to recognise that diplobacillary conjunctivitis is by no means infrequent in children. When all the cases in which the diplobacillus was present with the Koch-Week's bacillus are included, the figures show that 78 children out of 274 diplobacillary cases were affected, 28·46 per cent.

Gonin* found in Lausanne that diplobacillary conjunctivitis was rare in children. Axenfeld† states that the age varies between 10 and 57. Stephenson‡ states that it may occur at any age, even in newly born babies.

* Revue de la medicale de la Suisse-Romande (Fevrier et Mars, 1899). Reviewed in the Annales d'Oculistique, 1899, p. 78.

† Centralblatt für Bacteriologie Parasitekunde u. Infectionskrankheiten, vol. xxi, No. 1, January, 1897.

‡ Contagious Ophthalmia, p. 27.

Whilst a difficulty may arise in the differential diagnosis of Koch-Week's from diplobacillary conjunctivitis at the school period, such a difficulty can seldom occur in patients over 40 years of age, since in our series there are only two cases of Koch-Week's conjunctivitis—one of these had the diplobacillus associated—above that age, whilst diplobacillary conjunctivitis predominates at or beyond this age over every other form of conjunctivitis.

Interval Since Onset of Symptoms. — As regards the duration of the interval between the onset of symptoms and the patient's first visit, this to a certain extent varies with the age of the patient, for whilst in the majority of adults an interval ranging from 14 days to three months elapsed, in most of those at the school period the interval was shorter, generally about one week or thereby.

Previous Attacks, though not recorded in a large number of cases, are of sufficient frequency to be of diagnostic importance. They were noted in 61 of the 238 proved cases of diplobacillary conjunctivitis, and 30 times in the 78 unconfirmed cases. Of these latter, 13 from their clinical features would still be diagnosed as due to the diplobacillus. In two the diagnosis is almost certainly wrong. In 15 a diagnosis could only be made at random.

Others Affected.—The statement that others are affected is of little importance, from the fact that a large proportion of Koch-Week's cases give this history. In a case where there is doubt as to the differential diagnosis between Koch-Week's and diplobacillary conjunctivitis, the balance would be turned in favour of the conjunctivitis being due to the Koch-Week's bacillus by the fact that others were affected.

An example of the infectious nature of diplobacillary conjunctivitis is case 804, one of diplobacillary conjunctivitis, which attended on December 20, 1905. On the 27th of the following January her sister, aged 12, came, presenting symptoms which were characteristic of conjunctivitis caused by the diplobacillus. This micro-organism was found. This

is still better seen in the instance already mentioned in which five members of a family in the same house were affected with diplobacillary conjunctivitis; also in a family examined in March, 1906, in which the mother, a son and a daughter were bacteriologically proved to have diplobacillary conjunctivitis. Stephenson* mentions an outbreak of this form of conjunctivitis which affected about a dozen children.

Congestion of the Conjunctiva.—In about half of the proved cases of diplobacillary conjunctivitis (115 out of 238 cases) the palpebral conjunctiva alone was congested; this contrasts remarkably with Koch-Week's conjunctivitis, in which 33 out of 310 cases had the congestion limited to the palpebral conjunctiva. In children, however, according to our figures when only the palpebral conjunctiva is congested, the case, viewed from this symptom alone, is more likely to be one of Koch-Week's conjunctivitis than of diplobacillary, for of the 33 cases (palpebral conjunctiva alone affected) which occured in the Koch-Week's series, 23 occurred in children, whilst of the 115 cases which occurred in the diplobacillary series only 16 were in children. If infants are excluded the result is reversed—14 cases are due to the diplobacillus and 12 to Koch-Week's bacillus. It must, however, be borne in mind that there were 257 children with Koch-Week's conjunctivitis as against 54 with diplobacillary. While therefore the chances of a case of conjunctivitis in a child are very strongly in favour of its being due to Koch-Week's bacillus, these chances are greatly diminished when the palpebral conjunctiva alone is congested.

Amount of Discharge.—In the majority of proved diplobacillary cases the quantity of conjunctival discharge is small, 189 of the 238 cases. Of the 48 cases with a moderate quantity of discharge (Groups A and D) 14 occurred in children.

* *Loc. cit.*

Enlarged Follicles.—Enlarged follicles occurred in 20 of the 238 proved cases. Nine were in children and three in adolescents. In the cases of Koch-Week's conjunctivitis (310) there were 43 with enlarged follicles, of whom 38 were in children.

Conjunctival hæmorrhages, though rarely met with, do not exclude the possibility of a conjunctivitis being due to the diplobacillus; for in Case 469, an adult, aged 41, with symptoms present for two months prior to his seeking advice, the presence of the diplobacillus, which had been diagnosed, was confirmed by a film and culture. Conjunctival hæmorrhages were present. Also case 708, a patient aged 41, with symptoms for eight days, and with conjunctival hæmorrhages present. The conjunctivitis was not diagnosed as due to the diplobacillus, but this micro-organism was demonstrated in the culture. No film taken.

The presence of *chemosis or of membrane* on the conjunctiva would almost certainly exclude a diplobacillary conjunctivitis, for in none of the cases in the four groups A, B, C, D has either of these conditions been met with.

Swelling of the lids is noted in the majority of cases. In most instances it is much less marked than in the Koch-Week's cases.

Enlargement of the preauricular gland is less frequent in diplobacillary than in Koch-Week's conjunctivitis.

A *uniocular* diplobacillary conjunctivitis is uncommon (25 in 238). The interval since onset of the symptoms in the majority of these cases was short, in 15 of the 25 cases not longer than seven days; 12 of the 17 uniocular cases which were not diagnosed as diplobacillary conjunctivitis, but which proved to be so, occurred in children. In nine of these, symptoms had lasted not longer than seven days. We failed to diagnose a single case of uniocular diplobacillary conjunctivitis in children. A uniocular diplobacillary case which presented difficulty in deciding whether to include it in the series was—

Case 466, a male, aged 62, with a conjunctivitis of his left eye resembling that due to the diplobacillus, which micro-organism was proved to be present. The right eye showed no evidence of conjunctivitis, but the lower canaliculus was found to have been opened, and there was regurgitation of muco-pus from the sac when pressure was made on it. Pneumococci were proved by culture and animal inoculation to be present in the discharge from this lachrymal sac.

Corneal ulcers are met with in typical as well as atypical cases. They are noted six times in 238 cases which were bacteriologically proved to contain diplobacillus in the conjunctival discharge.

Character of the ulcers. In case 305 there were two small grey circular superficial ulcers near the outer margin of the right cornea. In case 281 there was a circular grey ulcer near the inner lower corneal margin. In case 544 the ulcer resulted from injury. In the remaining three cases (174, 102, 517) no details were given.

Of the four cases in which *phlyctenules* are noted, three occurred in children. In no single instance was a correct diagnosis of the diplobacillus made.

Angular conjunctivitis when present is almost pathognomonic, *vide* p. 469.

Based on a combination of these clinical features, it is possible to make a diagnosis with considerable exactness in the majority of cases of diplobacillary conjunctivitis especially when affecting adults. Thus of the 171 cases diagnosed correctly, 158 were in adults, whilst of the 67 wrongly diagnosed only 27 were in adults. A correct diagnosis is not so easily made in children, but our figures no doubt show a much higher percentage of failures in diagnosis than will result when it is appreciated with what frequency the diplobacillus occurs at this period of life. Of 54 cases of diplobacillary conjunctivitis in children a correct diagnosis was made only 14 times. A clinical diagnosis of Koch-Week's conjunctivitis was made in 19 of

the 54 cases, showing how the two varieties may resemble each other at this age.

Typical cases present little or no difficulty in diagnosis. In support of this, during the latter part of our inquiry, 18 cases presenting features supposed to be unequivocal were diagnosed clinically as diplobacillary conjunctivitis and marked "certain." In every instance the diagnosis was bacteriologically confirmed.

As typical cases of diplobacillary conjunctivitis we may cite—

Case 696, a female, aged 46, living in town, complaining of a gritty feeling in her eyes and gumminess of lids for 14 days; previous attacks; no others affected; only palpebral conjunctiva congested; discharge scanty; swelling of lids; symmetrical; angular conjunctivitis. Diagnosis: diplobacillus; film and culture gave diplobacillus.

Case 758, a female, aged 65, resident in town, difficulty in reading, gritty feeling in eyes and gumminess of lids for three months; no previous attacks; no others affected; only palpebral conjunctiva congested; discharge scanty; swelling of lids; symmetrical. Diagnosis: diplobacillus; culture and film gave diplobacillus.

Case 820, male, aged 41, resident in country, difficulty in reading, gritty feeling in eyes and gumminess of lids for three months. Previous attacks; no others affected; palpebral and ocular conjunctiva congested; discharge scanty; symmetrical; angular conjunctivitis. Diagnosis: diplobacillus; film and culture gave diplobacillus.

When all cases of conjunctivitis due to the diplobacillus are considered, there is a large group in which a diagnosis should be made with considerable certainty when based on a consideration of the various clinical characters, viz.:—

(1) Angular conjunctivitis, which occurs in about one-third of the cases and is almost pathognomonic.
(2) Age.
(3) Interval since onset of symptoms, which is of long duration in adults.

(4) Congestion frequently limited to the palpebral conjunctiva.
(5) Scanty discharge.
(6) Absence of conjunctival haemorrhages.
(7) A history of previous attacks.
(8) Cases coming from rural districts.
(9) Complaint of heavy lids.

In our series a diagnosis of diplobacillary conjunctivitis was made in 254 cases. In 176 of these, bacteriological confirmation was obtained—69·3 per cent. Viewed on the other hand from the bacteriological standpoint, of 243 proved diplobacillary cases 176 were correctly diagnosed, *i.e.*, 72·4 per cent.

Of the 78 cases wrongly diagnosed as due to the diplobacillus, seven proved to be due to Koch-Week's bacillus; six of these, the youngest of which was eight and the oldest 40 years of age, on reconsideration of their schedules, would still be diagnosed in a similar manner; this illustrates the impossibility in certain cases of differentiating clinically a Koch-Week's from a diplobacillary conjunctivitis. In the 7th case it would be difficult to form a diagnosis. A patient, aged 29, with symptoms present for four days; no previous attacks; no others affected; palpebral and ocular conjunctiva congested, a moderate quantity of discharge, lids swollen, and the condition uniocular. Diagnosis: diplobacillus. Film: Koch-Week's bacillus. Culture: Koch-Week's bacillus, staph. alb. and xerosis bacillus. The age is against the probability of its being Koch-Week's conjunctivitis, whilst the other conditions are compatible with a conjunctivitis due to either organism.

Nine of the 78 wrongly diagnosed cases were bacteriologically shown to contain *pneumococcus*; eight of these we should still diagnose as diplobacillary cases, as the clinical features are identical. The remaining one, Case 416, may have been a lachrymal one, in which case it should have been omitted. A female, aged 77, with symptoms present for

12 months, a history of others affected, congestion limited to the palpebral conjunctiva, scanty muco-purulent discharge, both eyes affected, with the right lower canaliculus slit.

Organisms were not demonstrated in six cases; in four of these no film was taken, and in another no culture was taken. In the six cases there is reason to believe that the diplobacillus was present, though the organism was not found. In support of this view, it may be noted that in five of the six cases only a film or a culture was taken, and that in all of these the quantity of discharge was small.

"*Other forms*" were found in 56 cases.

The difficulties of diagnosis, owing to treatment having been employed, is exemplified by the following:—

Case 814, a male, aged 25, with subjective symptoms of conjunctivitis present for 28 days, previous attacks, palpebral conjunctiva alone affected, discharge scanty; symmetrical, using "golden ointment." Diagnosis: diplobacillus. Film: cocci. Culture, nil.

Although there was no conjunctival discharge when seen by us, the next case was considered to be one of conjunctivitis due to the diplobacillus, but it was recognised that it might be impossible to obtain the specific organisms.

Case 779, a female, aged 63, complaining that the lids felt heavy, that they were gummed together in the morning, and that she had a feeling of sand in her eyes; symptoms had been present for two months, previous attacks, only palpebral conjunctiva congested, no discharge, symmetrical. Diagnosis: diplobacillus. Film: cocci. Culture: staphylococcus pyogenes aureus. For a similar reason, Case 776 was regarded in the same light.

During the latter part of our inquiry the rather frequent occurrence of diplobacillary conjunctivitis in children was recognised, and it was supposed that the following case belonged to this category. The diagnosis, however, of that organism was not confirmed; this shows the difficulty to be met with in arriving at a diagnosis in children.

Case 688, a female, aged 13, with the usual subjective symptoms of conjunctivitis for 14 days, previous attacks, only palpebral conjunctiva congested; discharge scanty, no others affected; symmetrical. Diagnosis: diplobacillus. Film: cocci. Culture, streptococcus pyogenes, staphylococcus pyogenes albus and aureus.

A somewhat puzzling combination of clinical characters was presented by Case 401, in which a diagnosis of the diplobacillus was made. In this case, in favour of the diagnosis of diplobacillus were the age, 34, residence in the country, previous attacks, and angular conjunctivitis. Against the diagnosis were the presence of conjunctival hæmorrhages, a moderate quantity of discharge and the short duration of symptoms—three days; it was symmetrical. Nothing but cocci was found. There was no culture.

In three of the 56 cases a diagnosis would be impossible. In four a diagnosis other than diplobacillus would be made, and in 49 the diagnosis would remain unchanged. Frequently cases are met with which are almost certainly due to the diplobacillus, but in which the discharge is either absent or so scanty at the time of examination that a sufficient supply of material for a satisfactory film or culture is not obtainable. The majority of these 49 cases belong to such a group.

Of the 67 cases wrongly diagnosed, which proved to be due to the diplobacillus, 31 were diagnosed as Koch-Week's conjunctivitis, and 19 of these were in children. Fourteen occurred in the early part of the series. On a reconsideration of the notes of these cases, it was found that the following case had points in favour of both Koch-Week's and diplobacillary conjunctivitis:—

Case 708, a female, aged 41, with symptoms of conjunctivitis for eight days, no previous attacks, others affected in the same house, both palpebral and ocular conjunctiva congested, scanty discharge, conjunctival hæmorrhages, swelling of lids, symmetrical. Diagnosis: Koch-Week's bacillus. The age and scanty discharge were the two conditions in favour of diplobacillary conjunctivitis, all the other conditions pointed to a Koch-Week's

conjunctivitis; no film was taken; in culture, diplobacillus and staphylococcus pyogenes albus.

That the clinical characters of diplobacillary conjunctivitis in a child may resemble those of Koch-Week's conjunctivitis is evident from this case—

Case 580, a child, aged 9, symptoms of conjunctivitis for 14 days, no previous attacks, palpebral and ocular conjunctiva congested, moderate quantity of discharge, lids swollen, preauricular gland enlarged, symmetrical. No film taken; in culture diplobacillus and staphylococcus pyogenes albus; also

Case 201, a child, aged 9, symptoms for two days, others affected in the same house, palpebral and ocular conjunctiva congested, scanty discharge, swelling of lids, preauricular gland enlarged, symmetrical, no film taken. In culture, diplobacillus and staphylococcus pyogenes albus; and

Case 431, a child, aged 12, with symptoms for four days, palpebral and ocular conjunctiva congested, a moderate quantity of discharge, swelling of lids, symmetrical, film and culture showed diplobacillus.

In eight of the 31 cases diagnosed as Koch-Week's conjunctivitis a different diagnosis would now be made. In three a diagnosis would be quite uncertain. In the remainder (20) the diagnosis would be unchanged. These, except two, were in children, which accentuates the difficulties of differentiating the two affections at this period.

Thirty-six cases diagnosed as "other forms" proved to be due to the diplobacillus. A few of these are as follows:—

Case 600, an infant of 3 weeks, with a history of discharge from both eyes since birth, palpebral and ocular conjunctiva congested, lids swollen, scanty discharge, symmetrical. Diplobacillus present in film and culture. Of four non-gonorrhœal cases occurring within the first few weeks of life, three were due to Koch-Week's bacillus and one to the diplobacillus.

Case 661, a syphilitic child in a much neglected condition, would give rise to insuperable difficulties in the clinical diagnosis

of the micro-organism which caused the conjunctivitis. A female, aged 4 months, with a history that the eyelids had been gummed together in the morning for the last two and a-half months, profuse conjunctival discharge, palpebral and ocular conjunctiva congested, lids swollen, symmetrical. The diagnosis of the micro-organism present was "other forms." In film, diplobacillus cocci and xerosis bacillus were present. In culture, staphylococcus pyogenes albus, aureus and xerosis bacillus.

It is believed that 21 of the 36 cases would now be diagnosed as diplobacillary. Of these 21 cases seven were in children, who had had previous attacks; 20 of them had scanty discharge; eight had symptoms present for a week or less. Five of the 36 cases would now be diagnosed as Koch-Week's conjunctivitis. In the remainder the evidence is so conflicting that a right diagnosis would be impossible, except by chance.

Bacteriology.—The discharge from cases in this group is frequently very scanty and is almost invariably poorer in cells than is the discharge from cases of Koch-Week's conjunctivitis. It is surprising how frequently the bacilli are found in relatively enormous numbers as compared with the number of cells. The material for a film may quite suitably be taken from the discharge collected at the caruncle. Good films can often be obtained in cases with no apparent discharge, by merely running the platinum loop over the caruncle and its neighbourhood. Bacilli when present in moderate numbers give rise to no difficulty in identification, but when few in number and when the bacillus xerosis is also present, one may at times have doubt. The bacillus xerosis, whilst smaller, sometimes resembles a diplobacillus. It is in such circumstances that the value of staining a film by Gram's method becomes apparent; still the recognition of one or two diplobacilli in a film would suffice for the diagnosis. The number of micro-organisms stands in no relation to the amount of discharge. Thus a scanty discharge may be teeming with micro-

organisms, whilst a moderate discharge may require careful searching of the film before the discovery of isolated diplobacilli. The bacilli are generally situated extra-cellularly, less frequently they occur intra-cellularly. They are from 2 to 4 μ in length and 1 μ in breadth. There may be two together joined end to end. We have never seen them arranged in chains. Their ends are rounded. Polar staining has not been noticed. They are not stained by Gram's method.

Cultures.—On ovarian agar after 24 hours at 37° C. round, elevated, semi-transparent, greyish colonies are readily visible. After 48 hours the increase in size is considerable, and frequently large colonies are met with displaying a pronounced central mammilla, with a greyish semi-transparent area around it. Such colonies are diagnostic. They are by no means constant. This cannot be due to defects in the media, for they have appeared on ovarian agar which was not giving satisfactory results with Koch-Week's bacilli, nor do the bacilli differ in mammillated from those in the other colonies. The mammillated colonies are almost invariably larger than the non-mammillated ones. Cultures after 48 hours may show abundance of involution forms (Photos. 4, 5, 6, 7, and 8). In older cultures their presence is constant. Sub-cultures from mammillated colonies do not reproduce this condition, which, in our experience, is limited to cultures made directly from conjunctival discharge. That the diplobacillus produces liquefaction of inspissated serum was shown repeatedly.

Of 238 bacteriologically proved cases of diplobacillary conjunctivitis, both a film and a culture were taken in 175; in these, 15 times the film and 12 times the culture gave a negative result. In cases with scanty or no discharge there is no evidence to show that a preference is to be given for a film rather than a culture, or *vice versâ*. In 19 of the 238 cases only films were taken, in 44 only cultures.

In the 78 cases diagnosed as due to the diplobacillus but not confirmed, 7 were shown to be due to Koch-Week's

bacillus and 9 to the pneumococcus. Of the remaining 62, in 38 both a film and a culture were taken, and in 32 of these discharge was scanty or absent. In 5 only a film was taken. In 19 only a culture. In all the discharge was either scanty or absent. In the 6 cases where no organism was found the discharge was scanty or absent. In only one of them was both a film and a culture taken. In Case 740, with angular conjunctivis, a film only was taken. As previously stated (*vide* pp. 478, 479), we now believe that 55 of the 62 cases were, in all probability, diplobacillary cases.

Gonorrhœal Conjunctivitis.—Of the 820 cases in the series, 21 were diagnosed clinically as due to the gonococcus; 18 of these were bacteriologically confirmed. Of the other 3, 1 was due to the diplobacillus and 2 to "other forms." In every case in which gonococci were found, a correct clinical diagnosis had been made. All the cases were in infants. Their ages ranged from 3 days to 2 months. Groenouw* investigated 100 cases of ophthalmia neonatorum and never once met with the diplobacillus.

In each of the 18 proved gonococcus cases the specific micro-organism was present in the film.

In 14 of the 18 cases a culture was taken, and in every instance a growth of the gonococcus was obtained.

As indicative of the facility with which growths of the gonococcus can be obtained on ovarian agar, in 24 cases (including the 14 already mentioned) in which a film showed the presence of the gonococcus, a culture was invariably obtained. The cultures maintained their vitality well, so that an indefinite number of sub-cultures could be obtained with ease.

The media for the growth of the gonococcus should be ovarian agar, hydrocele, or ascitic agar. The presence of blood derivatives is not essential.

Appearance of the culture:—After 24 hours' incubation at a temperature of 37° C., the gonococcus colonies are quite

* Die Augenentzündung der Neugebornen in klinischer u. bacteriologischer Hinsicht. Archiv f. Ophthalmologie, vol. lii, S. 1, 1901.

evident. After 48 hours, a luxuriant growth is present. The colonies are rounded, elevated, and semi-transparent, and have a grey appearance.

Tubercular Conjunctivitis.—The only case which occurred in the series, Case 419, was a female, aged 17, a farm worker, occupied chiefly in tending cows, with a history of redness and swelling of the right eyelids for three months, also gumming of the lids in the morning. There had been no pain. There was no difficulty, from the aspect of the conjunctiva, in making a diagnosis of tubercular conjunctivitis. There was also a depressed, bluish scar over the right preauricular gland. A swelling in this region had been previously lanced. Scrapings were taken and films made from the diseased conjunctiva. They were stained in the usual manner for tubercle bacilli, and after a prolonged search a single tubercle bacillus was found. The diseased conjunctiva was scraped and cauterised.

To clinch the diagnosis, a small piece of the affected tissue was inoculated in the groin of a guinea-pig. About five weeks later the groin glands were much enlarged, and there was an ulcer at the site of inoculation. After living for two weeks longer the animal was killed. The *post-mortem* examination showed several large superficial inguinal glands. The deep inguinal glands were also enlarged. The spleen was studded with tubercular nodules. The liver showed one or two nodules. In the lungs, especially the right one, were a number of tubercular deposits. Microscopically the affected tissues were found to contain numerous tubercle bacilli. A rabbit was also inoculated with a piece of the patient's affected conjunctival tissue. Generalised tuberculosis resulted.

On December 30, five months later, the patient reported herself, stating that she had no trouble with the eye. There was extensive scar tissue in the upper palpebral conjunctiva, but apparently no active disease.

Diphtheritic Conjunctivitis was met with once. Case 502, a male child, aged 2, was brought on account of "sore eyes."

The patient looked ill. Palpebral and ocular conjunctiva of both eyes were congested, and there was a moderate amount of muco-purulent discharge. A membrane extended over the whole of the left lower palpebral conjunctiva. Most of it was separated off by a platinum loop, with only a slight amount of bleeding. The conjunctiva thus exposed had a greyish appearance. A film was made; bacilli were present which resembled diphtheria bacilli. A culture gave colonies of diphtheria bacilli. A guinea-pig was inoculated with the culture material. Death resulted after 48 hours. The tissues were thickened at the site of inoculation, and, on removal of the skin in this region, numerous haemorrhages were seen. The adjacent glands were not markedly enlarged. The suprarenal glands were congested.

Subsequent course of the case: two days after the first visit the lids of the patient were somewhat swollen and the membrane extended over the conjunctiva of the upper and lower lids. He was removed to the fever hospital. Anti-toxin was administered and an uninterrupted recovery ensued.

Conjunctivitis not Proved to be Due to a Specific Organism.—After considering these various groups, there remain 114 cases in which a correct clinical diagnosis of "other forms" was made. The ground for making such a diagnosis was that, for various reasons, the conditions present made the isolation of a specific organism unlikely. The cases in this group are all of an atypical variety. A number had been rendered so by treatment with drugs, others by the eyes having been tied up. There was often an unreliable history, and random statements were made as to previous attacks and others affected. A number of the cases were young children sent by themselves. It is also to be remembered that a second bacteriological examination was not made in our cases. In 72 of the cases the affection was limited to one eye. In such cases symptoms had often been present for a long time. In nine of them the eye had been tied up, and, but for this circumstance, a diagnosis of Koch-Week's conjunctivitis would have been made. Example,

Case 729, a female, aged 9, with symptoms of conjunctivitis for 11 days; palpebral and ocular conjunctiva congested; moderate discharge; swelling of lids; uniocular. The affected eye had been tied up. Diagnosis: "other forms." Film: cocci; culture: streptococcus pyogenes and xerosis bacillus. Similarly,

Case 595, female, aged 9, with symptoms of conjunctivitis for a month, no previous attacks, palpebral and ocular conjunctiva congested, scanty discharge, lids swollen, uniocular, eye tied up. Diagnosis: "other forms"; no film taken; culture: staphylococcus pyogenes albus and aureus. It might be suggested that the tying up of the eye acted as a shield which prevented the affection spreading to the other eye; further, that the retention of the discharge under such suitable conditions as warmth and moisture, which favour the growth of organisms, caused so great proliferation of saprophytes that the relative proportion of the specific organism is diminished to such an extent that, on culture media, the luxurious growth of the non-specific organism chokes out the specific germ. As regards the value of films in such cases, it is suggested that the diminution of specific organisms, coupled with the marked increase in cellular elements, makes the number of such micro-organisms so small that their recognition is impossible. In none of the proved Koch-Week's cases is there an uniocular conjunctivitis in which the eye has been tied up.

After discounting as far as possible the elements of error, and reconsidering the cases, it seems reasonable to suppose that of the 114:—

(1) Forty-seven were cases of Koch-Week's conjunctivitis, *e.g.*, Case 8, a female, aged 12, with sore eyes for a week, previous attacks, others affected in the same house and elsewhere, only palpebral conjunctiva congested, scanty discharge, symmetrical. Diagnosis: "other forms;" no film taken; culture: staphylococcus pyogenes albus and streptococcus.

(2) Thirty-five were cases of diplobacillary conjunctivitis, *e.g.*, Case 92, a male, aged 33, complaining that his lids felt heavy and that he had difficulty in reading for three months; previous attacks, palpebral conjunctiva congested, scanty muco-purulent

discharge, enlarged follicles, symmetrical. Diagnosis: "other forms;" no film taken; culture: staphylococcus pyogenes albus.

(3) Two might be due to either of these organisms, and

(4) the remaining 30 are impossible of diagnosis. Some of these possibly should not have been included in our series. Some were in-patients who were engaged in dusty occupations.

Cases in which no Micro-organisms were Found.—Some of these had marked objective signs of conjunctivitis. On the other hand, in certain of the cases these signs were doubtful, as at most there was only very slight discharge and increased redness of conjunctiva. In such cases the diagnosis of conjunctivitis was confirmed by the history. As showing the importance of the history in making a diagnosis of conjunctivitis, we may note the case of a female child, aged 11 months, with a history of gumminess of lids for two days, others affected in the same house. Objectively there was only increased redness of the palpebral conjunctiva and hardly any discharge. Koch-Week's bacillus and the diplobacillus were found in both the film and culture. In another case, a child, aged one, there was scanty or no discharge, and the palpebral conjunctiva was reddened. These were the only objective signs. There was a history of the lids being gummed for one day, and of others in the house and elsewhere being affected. Koch-Week's bacillus and the diplobacillus were found.

Pneumococcus.—In 24 cases of the series diplococci were found unassociated with either Koch-Week's bacillus or the diplobacillus. Eight were diagnosed clinically as Koch-Week's cases, 9 were diagnosed as being due to the diplobacillus and 7 as "other forms"; on reconsideration of the latter, 6 we believe may have been Koch-Week's cases, and 1 a case due to the diplobacillus. Grouped in this manner, 14 presented symptoms of Koch-Week's conjunctivitis, and 10 of diplobacillary conjunctivitis. The ages of the 24 cases ranged from infancy to 57 years. As the symptoms may resemble those of diplobacillary or Koch-Week's con-

junctivitis, there are no clinical characters by means of which it is possible to make a diagnosis of the presence of the pneumococcus. It is possible that some, perhaps all, were due to Koch-Week's bacillus or the diplobacillus. In some of the proved Koch-Week's and diplobacillary cases a diplococcus was found. In 13 of the 24 cases, in which diplococci only were found, no film was taken.

The diplococcus, which we have presumed to be the pneumococcus, presented the following characters :—

(1) It exhibited a capsule in the films.

(2) On ovarian agar elevated dewdrop-like colonies were found, much larger than the Koch-Week's colonies, and, as a rule, larger than the streptococcus pyogenes colonies. Films made from such colonies showed a diplococcus staining by Gram, and with but little tendency to form chains. The virulence was tested in several cases, but the results were not constant. Mice were inoculated in a few cases with emulsions from the growth after an incubation of 48 hours. The animals did not always succumb. In fatal cases a capsuled diplococcus has been demonstrated in the organs. Diplo-streptococci have been met with in association with the staphylococcus pyogenes, the diplobacillus and Koch-Week's bacilli ; such diplo-streptococci have not been regarded as pneumococci. During the investigation 34 cases of lachrymal obstruction were examined ; in 25 of those a diplococcus similar to that already described was found. Inoculations on mice were made in 18 of the cases in which the diplococcus was found. In the majority a fatal result ensued. In those that died capsuled diplococci were present, but not invariably, in the heart's blood and spleen. The virulence of the cultures varied greatly, and the results were so inconstant that the identification of the pneumococcus by its pathogenic effect on mice was extremely unreliable.

Trachoma has not been met with in this inquiry.

Country Cases.—In the series of 820 cases, 75 came from districts outside the Aberdeen town boundary. In these

cases a distinction has been made, as far as possible, between those living in rural districts and those living in large villages or small towns. Of the 75 cases, two were proved to be due to Koch-Week's bacillus, and two to both Koch-Week's and the diplobacillus. The latter came from places quite near Aberdeen, and connected with it by tramway, car, and suburban railway trains. One of the former came from a large fishing village, the other from a town of more than 12,000 inhabitants. There is reason for believing that the infection by Koch-Week's bacillus in this last case occurred during her stay in Aberdeen, where she had been for some time before coming to the hospital. In the remaining 71 cases micro-organisms were found, as indicated in this table :—

	Cases.
Diplobacillus	37
Gonococcus	1
Pneumococcus	4
"Other forms"...	27
Tubercle bacillus	1
Nil	1

Thirty-six of the 71 cases came from rural districts, and none of these proved to be Koch-Week's cases.

To increase this limited number of country cases, others obtained from various sources have been added, thus, nine are from the cases examined in 1904; 94 cases in all had then to be considered. The age of 20 of these was under 20. In 44 of the cases the diplobacillus was found. The variety and relative frequency of organisms in the 94 country cases is represented thus :—

	Cases.
Diplobacillus	44
Gonococcus	1
Pneumococcus	6
Tubercle bacillus	1
Koch-Week's bacillus	2
Koch-Week's and diplobacillus	2
Nil	2

"Other forms" (staphyloccocus pyogenes, xerosis bacillus, streptococcus pyogenes, pseudodiphtheria bacillus) were found in the remaining cases.

In none of the 41 cases which came from rural districts were Koch-Week's bacilli found.

Early in this inquiry the absence of Koch-Week's cases from the country was noticed. It was thought that the relatively short duration of this form of conjunctivitis might partly account for their absence. In an endeavour to obtain information as to whether Koch-Week's conjunctivitis was scarce in the country, a number of medical friends in rural districts were asked as to their experience of conjunctivitis cases, and slides were sent to at least 22 of them, with a request for a film from any such case coming under their notice. Some of these slides were sent early in February, 1905. It it significant that only 18 slides were returned by the end of the year. On examination they were found to contain once Koch-Week's bacillus, thrice the diplobacillus, once the gonococcus, twice pneumococcus, twice nothing was found in the film; in the remainder only xerosis and staphylococcus pyogenes were discovered. One medical man from a rural district reported that cases of conjunctivitis were very scarce with him. Another reported, six months ago, that such cases were very scarce, and that he would be sure to send a specimen of the discharge if he got such a case. No film has yet been received from him. Another reported that he rarely if ever saw conjunctivitis in country cases. Another, five months after receiving a slide, reported that he had not yet had a case. Another wrote in July, 1905, that he had none of these cases just now. He referred to epidemics of conjunctivitis in which a number of people were infected by one another. "I will, however, send on anything that I can pick up." No slide has been received by 26th March, 1906. Another wrote, "It is a disease I very rarely see." Another wrote, "Conjunctivitis seems to be conspicuous by its absence here." Such statements as these have been made by the majority of country practitioners to whom we have

mentioned the matter. There is evidence therefore to show that the absence, in our series, of cases of Koch-Week's conjunctivitis from rural districts is at least partly accounted for by the rarity of their occurrence in these localities. There is little doubt that numbers of cases of diplobacillary conjunctivitis in the country never seek advice; this is less likely to occur in Koch-Week's conjunctivitis, which is usually a more acute inflammation. In this connection the following experiments are of interest as showing the greater vitality of the diplobacillus than of the Koch-Week's bacillus, when removed from the conjunctival sac; this may explain the comparative rarity of cases of Koch-Week's conjunctivitis in rural districts.

Erdmann* showed that when the discharge of diplobacillary conjunctivitis is placed on linen and exposed to room temperature, the bacillus can remain alive for as long as 14 days. In the few similar experiments made by us the organism was cultivated after four days. This is in marked contrast to the behaviour of Koch-Week's bacilli under the same conditions.

Seasonal Prevalence of Conjunctivitis.—When all town cases of conjunctivitis which occurred during the years 1899 to 1905 are tabulated, in accordance with the dates at which they came for treatment, and arranged in a monthly chart, it is seen that, apart from the constant fluctuation in numbers, there is, in five of the seven years, a distinct spring and autumn rise.

With regard to the form or forms of conjunctivitis which are responsible for this seasonal prevalence, information is only available from the cases, taken consecutively, in 1905. In that year the first rise occurred in March, the second in August, with an intermission in September, succeeded in October and November by the highest rise of the year.

The accompanying chart shows the monthly variation during the year 1905 in the number of cases of (1) all forms

* Ein Beitrag zur Kenntniss der Diplobacillen Geschwür, Klinische Monatsblätter für Augenheilkunde, May, 1905, p. 561.

of conjunctivitis; (2) diplobacillary conjunctivitis; (3) Koch-Week's conjunctivitis; (4) conjunctivitis associated with the pneumococcus; (5) gonorrhœal conjunctivitis; (6) other varieties of conjunctivitis.

The Spring rise is seen to be caused by an increase in the number of cases of conjunctivitis due to the diplobacillus, Koch-Week's, and "other forms," the greatest increase being in the diplobacillary cases.

The August rise is due to the Koch-Week's bacillus and diplobacillus, chiefly the latter.

The October-November rise is caused in the former month by an increase of the Koch-Week's bacillus, the diplobacillus, and "other forms"; in the latter month, during which the numbers still further increased, the Koch-Week's bacillus was wholly responsible. Saemisch* states that epidemics of Koch-Week's conjunctivitis are most frequent during the summer. Gonin† says that diplobacillary conjunctivitis is most frequent during hot, dusty summers.

In seeking to explain seasonal variations, the weather reports for the City of Aberdeen were consulted as to rainfall, wind, and temperature.

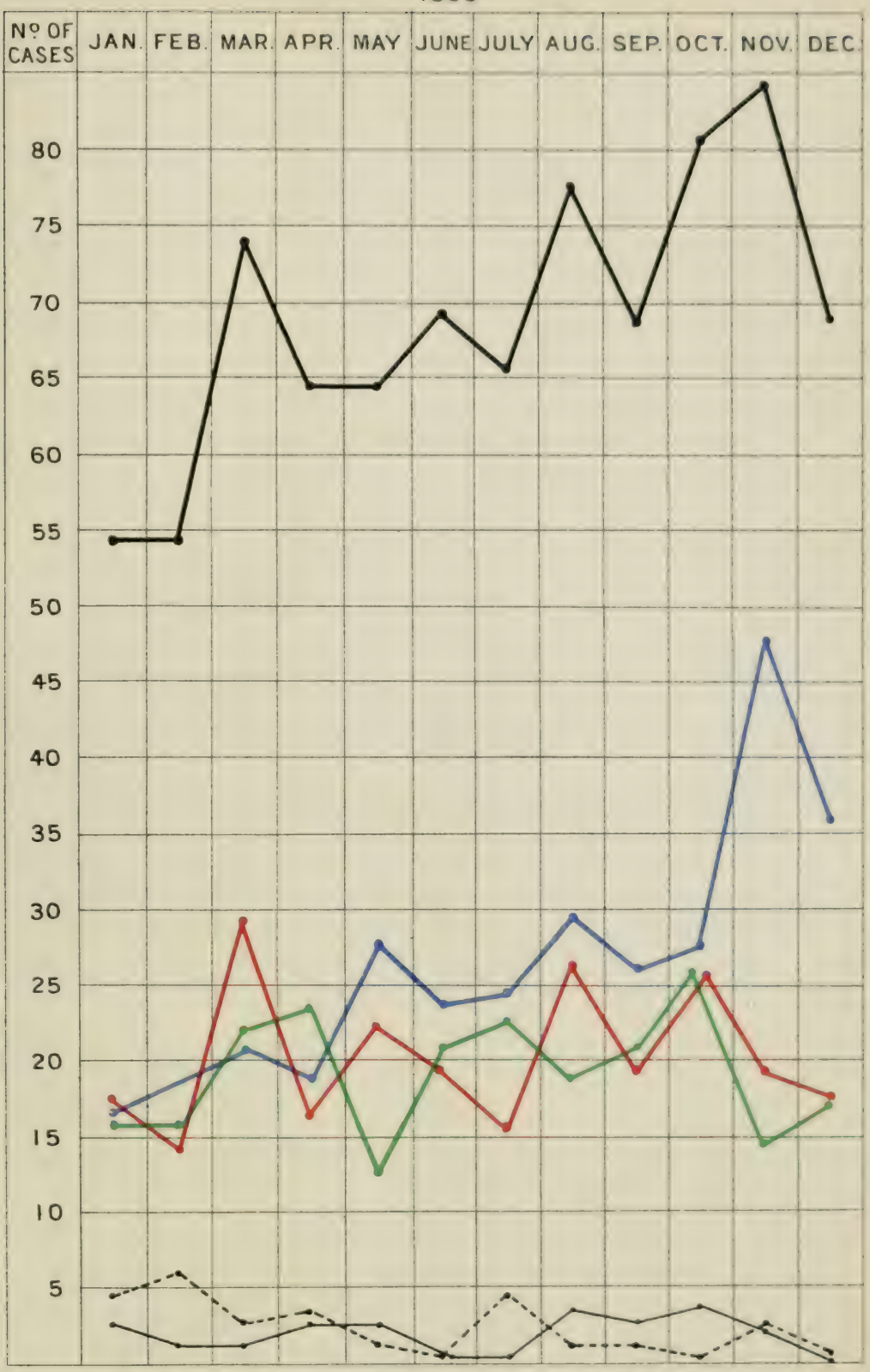
Rainfall: As a relationship between rainfall and the prevalence of conjunctivitis seemed to exist, the total rainfall for each year was taken; the total rainfall for each month was then taken and the percentage reckoned for each month with reference to its corresponding year. In 54 of the 84 months the amount of rainfall is in inverse proportion to the number of cases, *i.e.*, the greater the rainfall the fewer are the cases of conjunctivitis, and *vice versâ*.

The cases compared in the same way with reference to wind and temperature showed no evident connection.

Charts were prepared showing for each week in 1905 the number of cases of all forms of conjunctivitis, also of Koch-Week's cases by themselves, similarly diplobacillary and "other forms"; when these were compared with the weekly

* Graefe-Saemisch Handbuch, 2 aufl., article by Saemisch, p. 32.

† Graefe-Saemisch Handbuch, 2 aufl., article by Saemisch, p. 47.


1905
Nº OF CASES
JAN.
FEB.
MAR.
APR.
MAY
JUNE
JULY
AUG.
SEP.
OCT.
NOV.
DEC.
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
All forms of conjunctivitis (Country cases included)
Diplobacillary conjunctivitis
Koch-Week's conjunctivitis
Conjunctivitis associated with the pneumococcus
Gonorrheal conjunctivitis
Other forms of conjunctivitis

rainfall, temperature, and velocity of wind, no apparent connection could be established.

Conclusions.—As the result of this examination of a series of consecutive conjunctivitis cases, extending over a complete year, it is shown that the great majority of cases of conjunctivitis in this locality are due to the Koch-Week's bacillus and the diplobacillus of Morax-Axenfeld, the former predominating, although not largely.

The number of cases in which Koch-Week's bacillus was found was 310; diplobacillus of Morax-Axenfeld 274; gonococcus, 18; tubercle bacillus, 1; pneumococcus (unassociated with any of these micro-organisms), 24. Of the cases assigned to the group of "other forms," a large number, we believe, were either due to the Koch-Week's bacillus or the diplobacillus, although neither of these organisms was demonstrated.

Of the more important clinical characters by which a differential clinical diagnosis of the Koch-Week's bacillus is made, it was found that *conjunctival hæmorrhages* occurred in only 21·16 per cent. of the cases; that the *age* in 235 of the 284 cases was under 14 years, and that no case of conjunctivitis due to this germ came from a *rural district.*

The Koch-Week's bacillus, which was demonstrated in 310 cases, was associated with the diplobacillus on 36 occasions.

Recurrent attacks of conjunctivitis have been bacteriologically proved to be caused by the Koch-Week's bacillus. An interval elapsing between the attacks as long as 15 months has been noted.

In the majority of all cases due to the Koch-Week's bacillus a correct clinical diagnosis can be made, in this series, 86·4 per cent. Typical cases present no difficulty in diagnosis; on the other hand, there is a small number which are impossible of diagnosis.

Cultures of the Koch-Week's bacillus can be readily obtained when ovarian agar is employed; this medium is

superior to those in which other human body fluids are used.

Citrated ox-blood agar is excellent for the growth of Kock-Week's bacillus, and has the advantages that (a) the colonies are more conspicuous than on ovarian agar, (b) ox-blood can be readily obtained from a slaughter-house.

Of the more important clinical characters by which the diplobacillus can be recognised as the cause of a conjunctivitis, the appearances at the outer or inner canthus which have given rise to the term angular conjunctivitis are almost pathognomonic. Angular conjunctivitis, however, only occurred in 34·7 per cent. of the diplobacillary cases in this series.

Although the majority of diplobacillary cases occur in adults, 28·46 per cent. are met with in patients under 14 years of age.

Bacteriological proof has been obtained of the recurrence of diplobacillary conjunctivitis.

The infectious character of diplobacillary conjunctivitis was shown in instances where several or all of the members of a household were simultaneously affected.

The majority of cases of diplobacillary conjunctivitis came after symptoms had been present for a longer interval than in the case of those affected with the Koch-Week's bacillus; of the former, 164 cases came after an interval of at least two weeks—many after a much longer interval—and of the latter, 242 cases came after an average interval of 6·8 days. In diplobacillary cases the interval since onset of symptoms in children is shorter than in adults.

A correct clinical diagnosis of the diplobacillus can in the majority of cases be made, in this series 72·4 per cent.

Cultures of the diplobacillus are obtained without difficulty on ovarian agar.

The gonococcus can be readily grown on ovarian agar.

The presence of the pneumococcus in a case of conjunctivitis cannot be clinically ascertained.

In infants (one year or less) the commonest form of

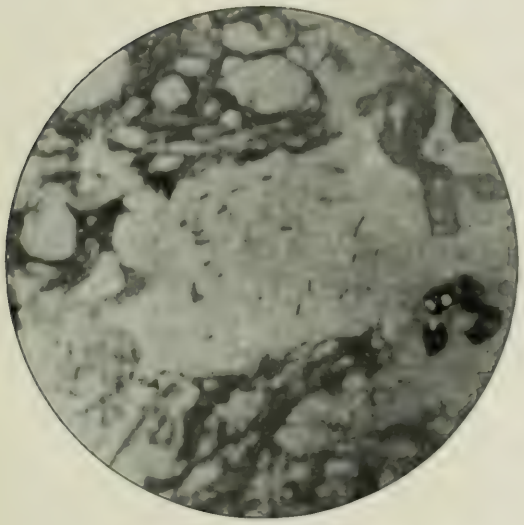


FIG. 1. Koch-Week's bacilli in conjunctival discharge. × 820.

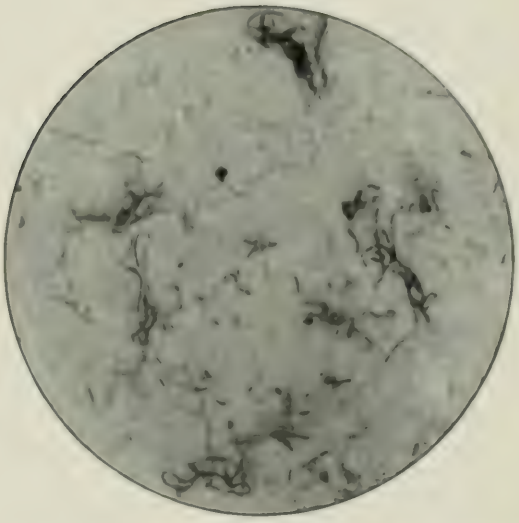


FIG. 2. Koch-Week's bacilli. Involution forms from a 96 hours' culture on ovarian agar. × 820.

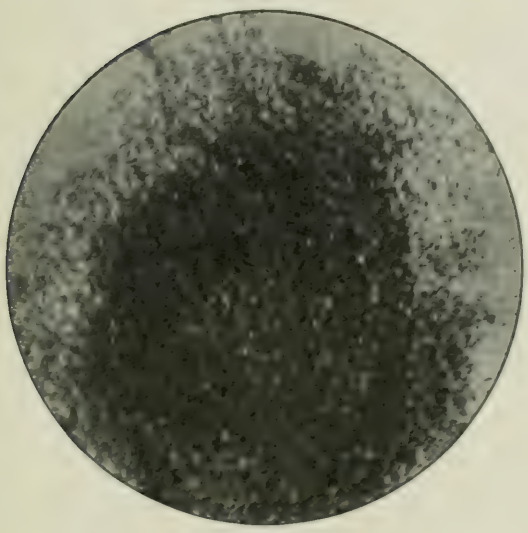


FIG. 3. Koch-Week's bacilli. Impression preparation of a colony from a 24 hours' culture on ovarian agar. × 820.

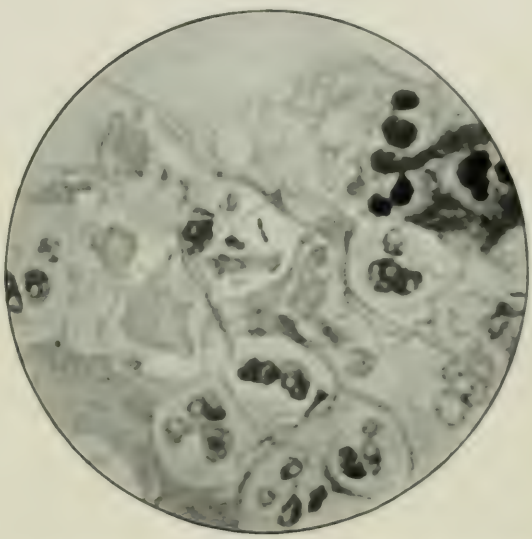


FIG. 4. Koch-Week's bacillus, with the diplobacillus in conjunctival discharge. Mixed infection. × 820.

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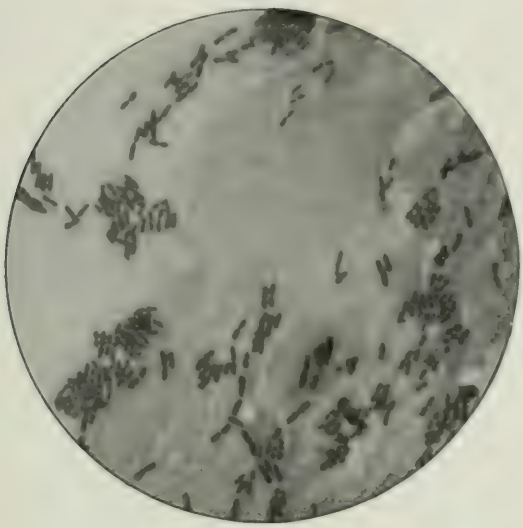

FIG. 5. Diplobacilli in conjunctival discharge. × 820.

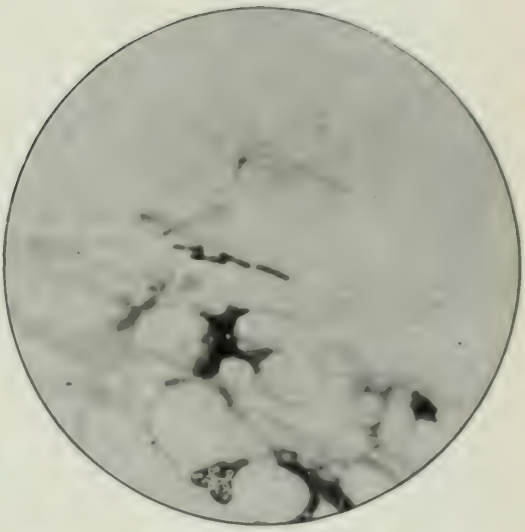

FIG. 6. Diplobacilli (long form) in conjunctival discharge. × 820.

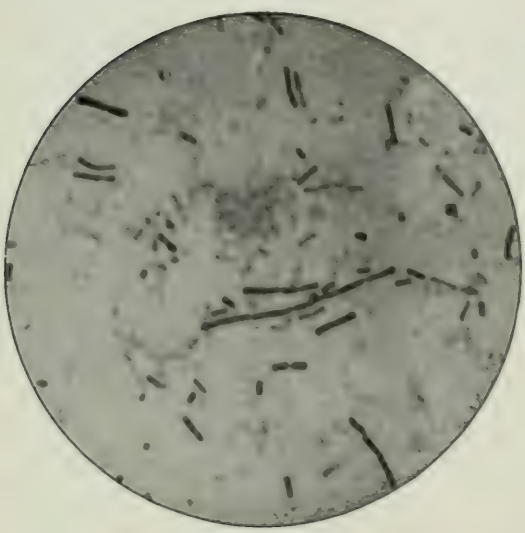

FIG. 7. Diplobacilli. Involution forms from a 132 hours' culture on ovarian agar. × 820.

FIG. 8. Diplobacilli. Involution forms from a 132 hours' culture on ovarian agar. × 820.

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conjunctivitis is that due to the Koch-Week's bacillus, the next in order of frequency is the gonococcus, and then the diplobacillus.

No definite relationship has been established between climatic conditions and the prevalence of the various forms of conjunctivitis.

By the kind permission of Professor Hamilton we have carried out the greater part of our bacteriological work in the Pathological Department at Marischal College. To those who have in any way furnished us with material for this investigation we are indebted, more especially to the surgeons of the Aberdeen Royal Infirmary, who have so readily given us every facility for obtaining the various fluids required.

RING SCOTOMA.

By W. Ilbert Hancock.

The subject of ring scotoma though not even mentioned in the majority of our text books is one of great interest, and its careful study, together with a faithful record of cases, might not improbably add much to our present knowledge of the distribution of the optic nerve fibres. Although there are a considerable number of recorded cases in ophthalmic literature, but few attempts have been made to deal exhaustively with the subject. Many theories have been advanced to explain the curious anomaly in the field of vision, and not a little confusion has arisen with regard to the cases which fall within this category.

Some have recorded under the term "ring scotoma" small crescentic defects in the field, others insular scotomata grouped in a more or less circular manner.

Although, no doubt, partial rings are only what one might expect, and are of great importance in the study of this condition, yet at the same time before interpreting such cases due care should be exercised in excluding the possibility of their being accidental occurrences.

With regard to the character of the scotoma, in position it practically always occurs in the intermediate part of the field of vision, the macular region and periphery remaining intact. Its outline, as a rule, is zig-zag, sometimes markedly so, though occasionally both its inner and outer limits may be quite regular.

The density of the scotoma frequently varies in different parts, some portions presenting an absolute, others a relative defect, or again, it may be relative throughout its whole extent.

The following cases have come under my personal observation, and for permission to publish Case 2, I am indebted to Mr. Treacher Collins :—

CASE 1.—Miss H., age 26, consulted me in November, 1904, complaining of defective sight in her left eye, and gave the following history:—

In August, 1902, whilst fastening the window in her bedroom during an exceptionally heavy thunderstorm she was, as she expressed it, "Struck and rendered unconscious by an extremely vivid flash of lightning which appeared to strike the left side of my face." The patient remembers nothing more until finding herself in bed some hours later.

Her friend, in whose house she was staying at the time, in reply to a communication from me, has favoured me with the following narrative:—

"Whilst sitting in the dining room of the ground floor I was startled by a loud scream from Miss H. in the room above, and on rushing upstairs found her unconscious on the floor. We put her to bed and applied hot bottles and restoratives, but it was quite an hour before she showed signs of returning consciousness. On recovery Miss H. complained that she was quite blind in both eyes, but thinking this was the result of the shock we thought little of it and no medical man was summoned."

On the following morning both eyes were much inflamed and the lids swollen, and though the sight in the right eye had quite returned the left was still blind. At the end of 48 hours the vision in the left eye commenced gradually to return, the improvement continuing for about 10 days, by which time the sight was as good as it has ever been since the accident.

There was no burning of the face, eyelashes or eyebrows.

On her visit to me, in November, she complained that on looking at an object with the left eye, the right eye being covered, it appeared to be surrounded by a circular shadow, which was constantly present and was darker in some parts than in others. Examination of the pupils showed the right to have a brisk normal reaction. The left contracted well to light, but the contraction was distinctly less well maintained than in the fellow eye, and after several oscillating movements the pupil came to rest slightly larger than the right.

$$V\begin{cases}\text{R.} & \bar{c} + 1 \text{ Dsph.} + \cdot 5 \text{ D}\downarrow = 6/4, \text{ J}_1 \\ \text{L.} & \bar{c} + 1 \text{ Dsph.} + \cdot 5 \text{ D}\downarrow = 6/6 \text{ partly, J}_1\end{cases}$$

The media and fundi in both eyes were perfectly normal.

A very careful examination of the affected eye under a mydriatic failed to demonstrate anything abnormal, *e.g.*, pigmentary disturbance or evidence of old neuritis.

Light sense tested with Bjerrum types.

R. $\bar{c}$ correction = 6/6.

L. $\bar{c}$ „ = 6/60 barely.

No history of night-blindness either before or after the accident.

Fields of Vision.—Right perfectly normal to both white and colours.

Left. Shown, Fig. 1.

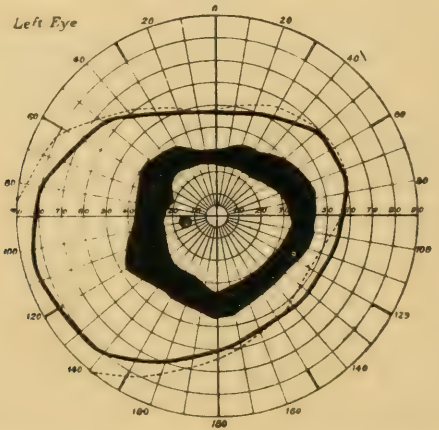

FIG. 1.—The ring scotoma was not so sharply defined as shown above, but was fringed by an area a few degrees in extent, in which there was a relative defect impossible to map out accurately. The colour fields compared with the fellow eye were markedly contracted.

The above field was taken on three different occasions at intervals of about a month and proved to be practically the same on each visit.

With regard to her family history her mother and father are living and well. She has two sisters and two brothers quite healthy, but one of the former suffered from chorea at nine years of age.

The patient was undoubtedly a girl of the neurotic type, but a careful examination of her nervous system failed to reveal anything abnormal, and I may add that she has never had an attack of unconsciousness before or since. I

at first thought that I was dealing with a functional disturbance, but the presence of a ring scotoma, involving a precisely similar portion of the field when taken on three different occasions after considerable intervals of time, the reaction of the pupil, and the defective light sense, point beyond doubt to there being some organic mischief.

Case 2.

Henry H., age 46, was first seen on September 27, 1903. He complained that the sight in the right eye commenced to fail about six weeks before, and since that time had gradually become worse. He was suffering from frontal headache and had completely lost his sense of smell.

No specific history; moderate smoker. Nervous system normal.

V. { R. Hand movements; not improved.
L. $\bar{c} + 1{\cdot}5 = 6/6$ $\bar{c} + 2{\cdot}5 = J_1$.

R. Pupil inactive to light or accommodation.

L. Pupil briskly active to both.

No pain on pressure on globe or in extreme movements.

R. Very little ophthalmoscopic change, but optic disc perhaps a little paler and more homogenous looking than the L.

L. Fundus and media normal.

Fields of Vision.

R. Large central scotoma peripheral field normal.

L. Normal.

Patient was treated with blisters to the right temple and potassium iodide internally, and the sight rapidly commenced to improve but never quite recovered.

On February 15, 1904, he again visited the Hospital.

V. { R. $\bar{c} + 1{\cdot}5$ Dsph. = 6/9 letters $\bar{c} + 2{\cdot}5 = J_1$.
L. $\bar{c} + 1{\cdot}5$ Dsph. = 6/6 $\bar{c} + 2{\cdot}5 = J_1$.

R. disc very pale, especially in temporal half, macula normal.

L. Fundus and media normal.

Field of Vision.

L. Normal.
R. (See Chart, Fig. 2.)

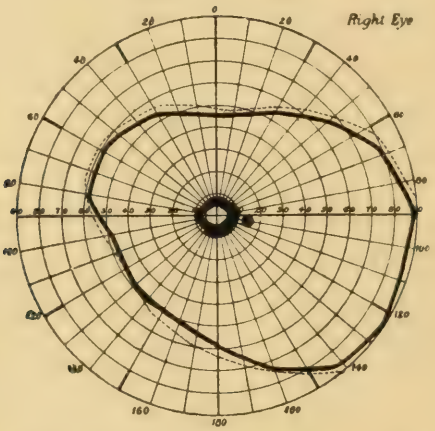

FIG. 2.—Peripheral field normal. A relative ring scotoma very definitely made out immediately surrounding the fixation point, roughly between the 3° and 10° circles.

CASE 3.

David H., age 28, came to the Hospital complaining of night-blindness. This trouble was first noticed eight years before, but

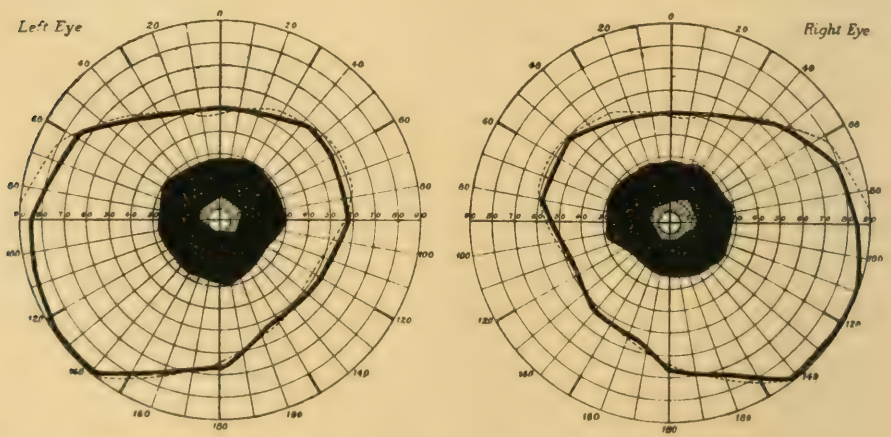

FIG. 3.—R. and L. fields taken with a 10 mm. white object, showing absolute ring scotoma between the 10° and 30° circles.

had become considerably worse during the last two years. He has one brother living, similarly affected, one sister, aged 20,

unaffected. An elder brother, who is dead, also suffered from night-blindness. Father and mother both died when patient was quite young, and he did not know if there was any blood relationship between them.

V. { R. = 3/60, J 20 not improved.
L. = 6/60, J 12 not improved.

Fields of Vision.—(See Fig. 3.) R. and L. Fundi almost identically the same. Retinal arteries very contracted, discs waxy; some sclerosis of choroidal vessels. Very marked "pepper and salt" fundus throughout with a very few small areas of branching retinal pigmentation in the extreme periphery.

Very marked granular appearance at each macula.

The case was in fact typical of the condition known as retinitis pigmentosa sine pigmento.

Many theories have been advanced to explain the ring-shaped defect in the field, some accounting for individual cases, others attempting to explain one and all by the same hypothesis. Of these we have the following:—

A. Which attributes the scotoma to a lesion of the retinal vessels and accounts for its ring-like character by the arched course of these vessels around the macula. (Hersing, Bull.)

B. Asserts that, owing to the anatomical arrangement of the venæ vorticosæ, the choroid at the equator of the eye-ball is more richly supplied with blood than other parts, and therefore more likely to become diseased. (Schön.)

C. Explains the scotoma as being the result of an exudation. The characteristic form is accounted for by assuming that the tension of the choroid and retina is less in the equatorial than in the antero-posterior direction, and therefore it is in the former direction that any exudation from the choroid would extend, and thus give rise to a circular defect in the field of vision. (Crzellitzer, Wettendorfer.)

D. Claims that ring scotoma is but the expression of impaired function of the retinal rods and can be demon-

strated in every case of night-blindness irrespective of causation. (Heinrichdorf.)

E. The equatorial belt of the fundus being situated at the point of meeting of the anterior and posterior ciliary system is not so well supplied as other parts of the eye. In fact, as Nettleship tersely expresses it, "the equator seems to be a sort of 'divide' between the two systems and to be not very efficiently served by either, whilst the current must be slowed or reversed in many of the anastomosing twigs. Given a congenital tendency (as in retinitis pigmentosa) to atrophy or hardening of the inner layers of the choroid it would probably tell first where the nutrient stream is weakest." (Gonin, Nettleship.)

F. That the cases are best explained by a retro-ocular lesion of the optic nerve. (v. Graefe, Leber, Burnett, Gallus.)

Of these theories the first three have so many obvious objections, and have already suffered so severely at the hands of their critics, that a further discussion of them is hardly necessary.

Ring scotoma has been met with in the following conditions:—

(1) Retinitis pigmentosa (including retinitis pigmentosa sine pigmento).
(2) Retinitis, choroiditis, and retino-choroiditis.
(3) Lesion of the optic nerve with or without optic neuritis.
(4) Glaucoma.
(5) Idiopathic night-blindness.
(6) Myopia.

Let us then consider these groups of cases in the above-mentioned order:—

(1) *Retinitis pigmentosa.*—It is in this affection that this form of scotoma most frequently occurs, and, indeed, it

seems highly probable that in the majority, if not in all, cases, it is one of the earliest manifestations of the disease. The scotoma is always progressive and has no definite relationship to the area of most marked pigmentation.

The vascular theory of Gonin and Nettleship was ingeniously devised to explain such cases, and was no doubt prompted by the fact that the scotoma occurs not infrequently in that part of the field which would roughly correspond to the equator.

The chief objections to the above theory are, in my opinion—

Firstly, that there are cases of retinitis pigmentosa in which the extreme outer limit of the ring scotoma in parts does not extend beyond the 15° circle (see Fig. 4).

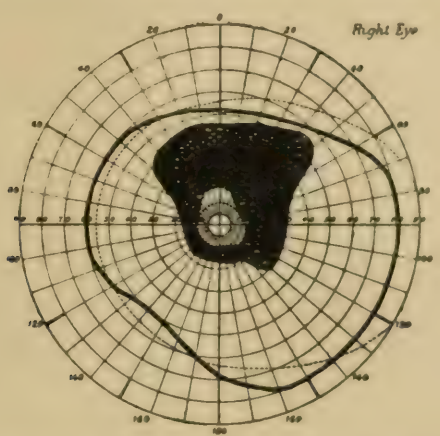

FIG. 4.—Field of vision from a case of retinitis pigmentosa (Gonin, Annales d'Oculistique, vol. cxxv, 1901).

Now, it has been proved by Hallidie and others that the equator of the eyeball is situated 67° from the fixation point. We have, therefore, a considerable distance between the extreme outer limit of a portion of the scotoma in Fig. 4 and the equator.

Again, in Case 3, in no part does the scotoma extend beyond 30°.

Gonin explains the varying position of the scotomata in the following way:—

"If the sclerosis of the choroidal arteries attacks simultaneously the anterior and posterior systems, it is in the intermediary zone at the equator that the scotoma will be situated. If, on the other hand, the posterior system is the first attacked, or, on the contrary, it is less severely attacked than the recurrent branches, then the scotoma will be situated more centrally in the former case, or more peripherally in the latter."

Even if we admit the "divide" to be comparatively broad and also admit that its anatomical position may be open to slight variation, yet it seems impossible to account for the position, assuming, as he does, that in such cases it is the terminal twigs of the posterior ciliary arteries that are first affected.

Secondly, the outline in a number of the scotomata in retinitis pigmentosa is perfectly regular, and it is hardly conceivable that a degenerative condition affecting a complex vascular network could spread in such a perfectly even manner.

Thirdly, the 15 to 20 ciliary arteries perforate the globe in a circle round the optic nerve, yet in all the cases pictured it is strikingly evident that the scotoma is concentric with the point of fixation, not with the blind spot.

(2) *Retinitis, Choroiditis, Retino-Choroiditis.* — It is a striking fact that certainly in many cases of ring scotoma occurring in the above conditions, the defect in the field of vision does not correspond to the part of the fundus seen ophthalmoscopically to be diseased.

Again, the scotoma may vary considerably without a variation in the ophthalmoscopic picture, and in other cases it has disappeared, in spite of the fundus disease being of a progressive character. (Gallus.)

In almost all there has been a definite specific history, in fact some authors have stated that a ring scotoma occurring in retino-choroiditis is pathognomonic of syphilitic disease. Nettleship explains the ring scotoma in this group of cases by assuming arteritis of the equatorial twigs of the choroidal

arteries, either of the posterior or anterior system, or both. This explanation is not satisfactory for all cases, notably one of syphilitic retinitis comparatively recently described by Handmann.

Female, age 45.—Specific history. No night-blindness.

V { R. = 6/9.
  { L. = 6/6.

R. Circular area of retinal pigmentation, including disc and macula within it. It approaches closely to the disc on the nasal side and almost touches the macula on the temporal. Disc somewhat blurred in temporal half, good colour. Arteries slightly narrowed. Periphery of fundus normal. Field shows a ring scotoma concentric to the fixation point and lying entirely between the 5° and 30° circles. Field for white normal.

L. Fundus change much the same as right, but pigmentation not nearly so pronounced, and its ring-like distribution incomplete, being most marked on nasal side of disc, less marked on the temporal side and absent above and below. Arteries and disc normal. Field shows a crescentic absolute scotoma, situated roughly between 10° and 20° around the upper half of fixation point. Peripheral field taken in a dull light quite normal.

Here we have a case in which the outer limit of the scotoma does not extend beyond the 30° circle, and cannot be explained by assuming an arteritis of the "equatorial twigs."

This is also an interesting case as being one of the instances in which the defect in the field corresponds fairly accurately in the right eye with the diseased area in the fundus, but it will be noticed that there is no such correspondence in the left eye.

(3) *Lesions of the Optic Nerve with or without Optic Neuritis.*—There are cases recorded of ring scotoma in which the fundus has been perfectly normal, and which clinically were typical of the class known as retrobulbar neuritis. Burnett, many years ago, described a most interesting case which is extremely difficult to explain by any other hypothesis than a tract or chiasma lesion.

Male, age 55.—Syphilis two years before his first visit. A year before had an attack of inflammation in both eyes with acute pain.

V { R. = 4/30 not improved.
  { L. = 4/30 ,,

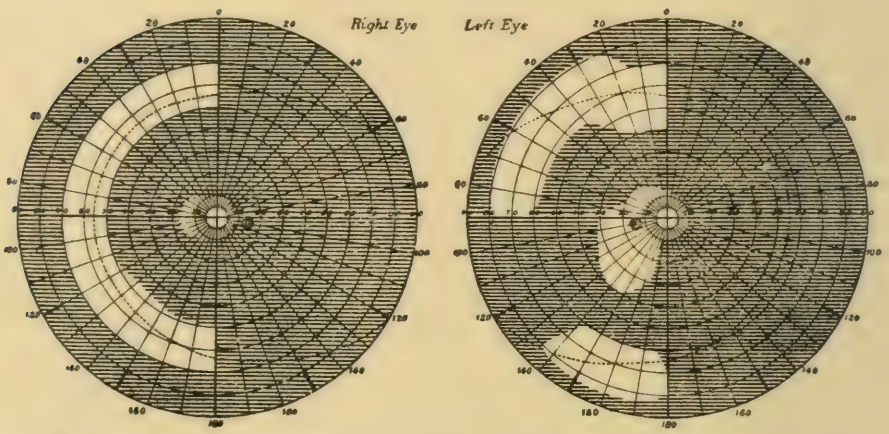

FIG. 5.—Burnett's case. Fields of vision taken on first visit of the patient, showing hemianopia and presence of a ring scotoma in retained half of the field (Trans. Amer. Ophth. Soc., 1887).

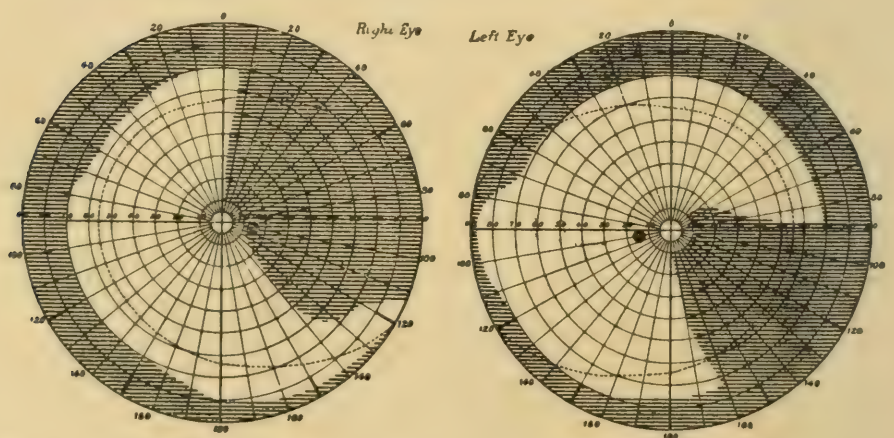

FIG. 6.—Fields taken a month later. The ring scotoma has entirely disappeared and there is a partial recovery of the hemianopic field.

R. and L.—Some posterior synechiæ with spots of pigment on lens capsule. Fine vitreous opacities. No choroiditis. Retinal vessels normal. Fields (Figs. 5 and 6). Patient treated by inunction of mercury.

A fortnight later severe headache and numbness on left side

of body : Vitreous clearer. Fundus normal. Eight months later V. R. and L. = 4/15. Vitreous clearer.

The patient was watched for nearly two years, the fields showing varying forms, the vision greatly improving. When last seen the left field was practically normal, and the right showed some irregular peripheral contraction with two small insular scotomata. A note of the fundus at this time says there was some disturbance of pigmentation down and out in right, reaching nearly up to the macula. In left—patch of pigmentary change up and out six to eight disc diameters from nerve head.

Evidently there was here a complete loss of function of the left tract with, at the same time, implication of the intermediate fibres in the right.

The dividing line between the two halves of the field of vision is typical of hemianopia, namely, strictly vertical with a reëntrant angle at the point of fixation, leaving central vision intact. Lastly, we have the changing forms in the field, which could only be explained by a varying pressure on the tracts or chiasma.

It might possibly be argued that in the above case the hemianopia was due to a tract lesion, and the ring scotoma to a retinitis.

Against this, however, it is extremely unlikely that a retinitis could cause such a perfectly regular circular scotoma as was present in the right eye.

Burnett, in his communication, directs attention to Bunge's assertion that the macular bundle supplies the central area of the retina for an oval space of approximately 20° in the horizontal and 10° in the vertical direction. He further points out that in the two cases recorded by him the area of central vision remaining unaffected is almost the exact counterpart of the central scotoma met with in circumscribed retrobulbar neuritis.

A case not unlike the above has been recorded by de Schweinitz :—

The visual fields in this case were taken at irregular intervals over a period of five years. When first seen, there

was an absolute scotoma in the left lower quadrant of each eye. Four years later the fields showed in addition to the previous lesion a typical right lateral hemianopia. Five years after the first visit the large defects in the fields had cleared up, and there was now present a slight peripheral contraction, and a ring scotoma in each eye, roughly between the 10° and 30° circle.

The fundi were perfectly normal throughout.

From our present incomplete knowledge of the distribution of the optic nerve fibres it is extremely difficult, if not impossible, to explain how the annular scotoma is brought about in retro-bulbar neuritis, using the term in its broadest sense. A careful study of the most recent experimental work on the subject by Usher and Dean, and by Parsons, shows that we only know of one specialised bundle in the optic nerve, namely, that composed of the fibres supplying the macula. Yet the remaining fibres of the nerve have a fairly definite arrangement, and it is generally accepted that those most peripherally situated supply the intermediate portion of the retina, and those more centrally placed are distributed to the peripheral retina. This arrangement is fairly constant throughout the whole length of the optic nerve, modified only by the varying position of the macular bundle which, as is well known, occupies a wedge-shaped area at the temporal side of the disc, and gradually takes up a central position in the nerve before reaching the bony optic foramen.

A lesion, therefore, destroying the peripheral fibres of the optic nerve would give rise to a defect in the intermediate field arranged in a circular manner.

Gallus, in advocating the retrobulbar origin of this form of scotoma, puts forward a new theory of the pathology of retinitis pigmentosa.

He assumes that the primary cause is compression of the optic nerve and ophthalmic artery at the bony optic canal from chronic periostitis. At this point the macular bundle is centrally situated, and the fibres of the optic nerve, which

are here peripheral, are distributed to the intermediate portion of the retina.

The first effect, therefore, of the pressure is to destroy the function of the most superficial fibres which gives rise to a ring scotoma.

The narrowing of the retinal vessels he explains by a like compression of the ophthalmic artery. If the pressure is continued a gradually increasing atrophy of the nerve takes place with a corresponding peripheral contraction of the field of vision, the macular bundle being here centrally placed is therefore the last to suffer.

Lastly, he explains the retinal pigmentation so characteristic of the disease as resulting from the degeneration and thickening of the ciliary arteries, which he asserts is the necessary concomitant of long-continued pressure on their parent trunk. This theory is unsupported by any pathological data, and his deductions as to the effect on the retinal and ciliary vessels of compression on the ophthalmic artery seem to me unsatisfactory.

(4) *Glaucoma.*—It would appear, from the paucity of cases recorded, that ring scotoma occurs very rarely in glaucoma, and, as far as I have been able to ascertain, there are only 7 cases mentioned in ophthalmic literature (Noyes, Mittendorf, Handmann, de Schweinitz, Zentmayer and Posey. Pflüger, Bjerrum).

Of these, Handmann's is the most recently described:—

Female, age 59. Sought advice for a "shadow" in the right eye.

R. $\bar{c}$ correction = 6/6, J_1 T*n*.

L. $\bar{c}$ correction = 6/6, J_1 T*n*.

R. Shallow anterior chamber. Very marked pathological cupping of disc, with some pallor.

L. Shallow anterior chamber. Pathological cupping of disc, but not so extensive as in fellow eye. Nerve good colour.

R. Field showed a ring scotoma between the 10° and 20° circles with some concentric contraction in the field for white.

L. Field normal.

Several suggestions have been made to explain the scotoma in this disease. Thus it has been attributed to a mere accidental occurrence, to an invisible affection of the rods and cones, and lastly by Bjerrum to the destruction of the fibres in the papilla at the margin or sides of the excavation.

The loss of field in glaucoma is the result of pressure either on the nerve fibres or retinal vessels, or both; and compression of the nerve fibres against the unyielding scleral canal implicating only those most peripherally placed at the disc, might possibly explain a case such as Handmann's.

The recorded cases are so few that it makes it extremely difficult to offer a satisfactory explanation, and it is quite possible that if the fields of vision in cases of glaucoma were more systematically searched within their boundaries with a small test object, ring scotoma would be more frequently found in this condition.

With this object in view, Bjerrum's method of testing the field of vision would, no doubt, be an admirable one. Unfortunately, however, the length of time required to carry it out satisfactorily renders it, at least in hospital work, quite impracticable.

(5) *Idiopathic Night-blindness.* — Heinrichdorf, in his recently published paper, after accepting as proved that the rods are the basis of vision of low intensity, gives the fields of 11 cases which he has examined. Retinitis pigmentosa (6), retinitis pigmentosa sine pigmento (1), idiopathic night-blindness (1), monocular optic neuritis (1), neuro-retino-choroiditis (1), disseminated choroiditis with retinitis pigmentosa (1).

He shows that in some of these cases the field of vision was perfectly normal when taken in a bright light, but when taken with a dull illumination there was present a well-marked complete or partial ring scotoma. He argues that in all cases of night-blindness, whether congenital or acquired, a ring scotoma can be demonstrated if the field of vision be taken in a dull light. Unfortunately, the

descriptions of his cases are meagre, practically confined to vision and diagnosis, and he gives no explanation of why the scotoma should take this form. It is therefore difficult to judge of the value of this communication.

(6) *Myopia.*—With regard to the ring scotoma occurring in the above condition, I can find but few references to the subject.

Weiss has described cases of both relative and absolute ring-shaped defects which he ascribes to extension of the blind spot above and below; the prolongations occasionally pass in a crescentic manner temporalwards, and meeting to the outer side of the fixation point enclose the latter within the circle.

Wettendorfer, in a lengthy communication, arrives at the following conclusions:—

(1) In the majority if not in all cases of myopia above 6 D, if the field is mapped out carefully with a 5 mm. object in a good light, there will be found concentric zones in which there is either a relative or absolute scotoma.
(2) The scotoma is always negative.
(3) The commonest situations are—

(*a*) Prolongation of the blind spot.
(*b*) In the periphery, leaving only a narrow belt a few degrees in extent between it and the extreme peripheral limits of the field of vision.

Between these two situations not infrequently other concentric scotomata may be mapped out so that there may be as many as five rings, the field resembling a target.

(4) The abnormalities of the field are entirely independent of changes in the fundi, and the greatest precautions were taken to guard against the scotomata being due to fatigue.

So far as I know, these results have not been verified by any other observers, and one must hesitate before accepting them.

Of the three cases described by me at the commencement of this paper, Case 1 is of great interest, from a speculative point of view, not only as to the site of the lesion, but also as to its causation.

Lightning injuries of the eye are but seldom met with in this country, and with regard to the *modus operandi* of the electric energy, Collins, in a communication in the Trans. Ophth. Soc., suggests that it may act in one or more of three different ways:—

(1) By the heat rays producing, *e.g.*, burns of the lids and conjunctiva.
(2) By the chemical ultra-violet rays giving rise to symptoms similar to those met with in snow-blindness and ophthalmia electrica, *e.g.*, blepharo-spasm, conjunctival hyperæmia.
(3) By electrolytic action or concussion giving rise to changes which can be reproduced on animals by shocks from Leyden jar batteries, *e.g.*, paralysis of ocular muscles, retinal hæmorrhages, optic atrophy, ruptured choroid, and detached retina.

There can, I think, be no doubt that the organic mischief in the above case was brought about by the lightning, and from the entire absence of ophthalmoscopic fundus disease it is fair to assume that the site of the lesion was probably in the optic nerve. On the other hand, it must be remembered that Birch-Hirschfeld has shown that the ultra-violet rays have a marked effect on the ganglion cells of the retina, which at once suggests the possibility of there being a primary retinal lesion; but even accepting this as a possibility, we have still to account for its circular distribution—an insurmountable difficulty.

Case 2 is of unusual interest from the position of the

scotoma, which apparently involves part of the macular bundle, and it seems to me that the most probable explanation is that it is due to a clearing up of the mesial area alone of the large central scotoma, which was a prominent feature on the first visit of the patient.

CASE 3 is described to show that the ring scotoma in retinitis pigmentosa does not always correspond to the equator.

To summarise this communication: If we exclude the very rare cases of glaucoma, idiopathic night-blindness, and myopia as requiring further verification, the cases fall into two main groups.

A. Those cases in which the retina or choroid is diseased:—

(1) Those in which the diseased area of the fundus corresponds with the scotoma in the field.
(2) Those in which there is no such correspondence.

B. Those cases in which the fundus to ophthalmoscopic examination is perfectly normal.

These groups of cases are explained by two separate hypotheses. The one invokes an *intra*-ocular, the other an *extra*-ocular causation. Those who favour the former explain the scotoma in retinitis pigmentosa upon the generally accepted pathology of that disease, viz., that the primary lesion is a sclerosis of the choroidal vessels, and account for the ring by the Gonin-Nettleship hypothesis. In the cases of retino-choroiditis a similar interpretation is given, but no attempt is made to explain cases in which the fundus disease does not correspond to the position of the scotoma.

Lastly, those cases in which the fundus is perfectly normal are either ignored or dismissed by assuming that there is an invisible lesion of the sentient retinal layer, which to my mind is quite inadmissible.

With regard to the second hypothesis (the extra-ocular

causation), the fact that we have a definite group of cases of undoubted retrobulbar neuritis with ring scotoma, but without fundus change, is to me positive proof that a pure nerve lesion will account for this ring-like defect in the field of vision, and the peculiar correlation of groups of fibres in the optic nerve with concentric areas in the retina gives a reasonable confirmation of this view.

This retrobulbar view could also be applied to those cases of ring scotoma in retino-choroiditis where the defect in the field does not correspond with the area of fundus change, and it is strongly supported by the cases of Burnett and de Schweinitz with hemianopia.

In retinitis pigmentosa I have shown that to me the Gonin-Nettleship view fails to explain the ring defect in many cases.

Lister, in describing the microscopical appearances of a case of retinitis pigmentosa, after pointing out that there is no sclerosis in the choroidal arteries, says :—

"Some hold that these changes are brought about by primary vascular disease either of the retina or choroid. But the concentric defect corresponds with a *nerve distribution* rather than a *vascular distribution*, and therefore I think we must look for a degeneration commencing primarily in the nervous tissues rather than in either vascular system."

This is perhaps too much to assume till further evidence is at hand, but it receives support from the definite retrobulbar cases with ring scotoma mentioned above.

In conclusion, my best thanks are due to Dr. Markus, to whom I am greatly indebted for helping me with the foreign literature on this subject.

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FURTHER CASES OF THROMBOSIS OF THE CENTRAL VEIN.

By George Coats, Curator.

In a former paper* on the subject of thrombosis of the central vein I showed that the pathological examination of affected eyes had so far led to confusion rather than to clearness. No fewer than six different lesions had been described by different authors as the essential basis of a very well-defined clinical entity. I reported four cases, in the hope of adding to the data available for retaining or rejecting this multiplicity of explanations, or, if possible, of bringing the several lesions into line under one dominating factor. At the same time the opinion was expressed that this could not yet be done with certainty, and that a greater number of fully-examined cases, with transverse serial sections through the region of the nerve entrance and lamina cribrosa, were required. Shortly afterwards I was able to report another case,† and since then I have collected 11 others, upon which the present paper is based.

An important contribution to the subject has been made by Harms‡ in a long and excellent paper. This author has reported two cases of arterial and 10 of venous obstruction. Of the latter, one seemed to be due entirely to obliteration of the vein from endo- and mesophlebitis, without thrombosis. One was due to an organised thrombus, apparently associated with a normal vein wall. Three were due to thrombosis associated with disease of the vein wall, the coagulum being laid down at the site of greatest disease in one, somewhat farther up the nerve in the other two. In one of these two the thrombus was canalised, the case resembling Case 2 of my former paper, which was the first recorded example

* R. L. O. H. Rep., vol. xvi, pt. i, p. 62, 1904.
† Trans. Ophth. Soc., vol. xxiv, p. 161, 1904.
‡ Arch. f. Ophth., vol. lxi, pt. i, p. 1.

of this condition. In two there was a thrombus in the vein, associated with advanced endarteritis in the artery; in one of these there was also a thrombus in the artery. In three cases no obstruction was found in the central vein, but in two of these the nerve entrance was cut longitudinally, and in one the nerve was divided very close to the globe, and there was a deep glaucomatous cup, so that almost no part of the central vein was available for examination; in two some of the retinal veins were thrombosed. From the consideration of his own cases, and of those recorded in literature, Harms comes to the conclusion that the following lesions have actually been proved by pathological examination in cases clinically diagnosed as "thrombosis of the central vein"; (1) Thrombosis of the vein. (2) Disease of the vein wall (endo- and mesophlebitis). (3) A combination of these two. (4) Very exceptionally (Yamaguchi) compression of the vein from without. He is also inclined to admit thrombosis of the retinal veins without obstruction of the central vein. He regards with the gravest suspicion (and in this I fully agree with him) recent attempts to explain such cases by lesions on the arterial side of the circulation. Where the whole course of the vein, and especially that part of it which traverses the lamina cribrosa, has not been examined in transverse sections, there is a strong probability that the essential lesion has been overlooked. The endarteritis may indeed be the cause of the ophthalmoscopic appearances, but not directly, only by slowing the blood current, and so favouring the deposition of a thrombus in the vein; this again will react prejudicially on the arteries. If such a thrombus is *not* formed in the vein, and if the endarteritis progresses sufficiently, the picture of obstruction of the artery is produced, not that of occlusion of the vein. This also has been definitely proved by pathological examination, Galinowsky,* Harms,† Coats,‡ etc.

* Arch. f. Augenh., vol. xliii, p. 183, 1901.

† *Loc. cit.*, Case 1.

‡ R. L. O. H. Rep., vol. xvi, pt. iii, p. 262.

Another example of a canalised thrombus has been reported by Sidler Huguenin.* The endothelium of the artery was extensively detached, and lay coiled up in the centre of the lumen, an appearance which the author believed to be due to stripping up by the blood current, such as occurs in dissecting aneurism. The thrombosis of the vein was supposed to be due to slowing of the blood current from this cause. It is by no means certain, however, that the condition in the artery was not in part an artefact. A somewhat similar condition of affairs will be described in some of the cases mentioned below.

Baquis† has also reported a case in which an organised thrombus was found in the vein in the region of the lamina cribrosa. In all these cases glaucoma followed the thrombosis at a longer or shorter interval.

Bartels‡ has studied the condition of all the ocular vessels in glaucoma, but without throwing any new light on the connection of that condition with thrombosis of the central vein.

Cases.

In the following cases the method of examination was the same as that described in my former paper. The eyes were all preserved in formalin, except where otherwise stated. The globe was cut in serial section, every fifth to tenth being mounted (in different cases), and others in the intervals where necessary. The nerve and nerve entrance were excised, and cut in transverse serial sections throughout their length. In addition to the ordinary staining methods, Weigert's elastic tissue stain was used, and rendered much assistance. I omit all unimportant details in the descriptions.

Case 1.—*Thrombosis of right central vein of doubtful, but probably short duration. No albuminuria or evidence of*

* Arch. f. Augenh., vol. li, p. 27, 1904.
† Festschrift f. Hirschberg, p. 33, 1905.
‡ Zeitsch. f. Augenh., vol. xiv, p. 103, 1905.

arteriosclerosis. Glaucoma. Excision about three weeks after its occurrence. Left eye normal throughout. In the bisected eye very numerous retinal hæmorrhages with large tortuous veins. Loosely reticular cellular mass in central vein in anterior layers of the lamina cribrosa. Obstruction terminated posteriorly by the accession of a collateral branch. Endarteritis in the central artery. Moderate changes in the retinal vessels. Corneo-iridic angle more occluded on the temporal than on the nasal side.

I am indebted to Mr. Lawford for the material and clinical notes of this case:—

A gentleman, aged 60, first consulted Mr. Lawford in January, 1903, when vision in each eye was 6/5, with a low hypermetropic correction. In September, 1904, he discovered that the sight of the right eye was defective. The vision at that time was 6/36; the papilla was thought to be somewhat cupped, but its colour was good; the tension was doubtfully raised; the field of vision was full. In December, 1904, a few spots of hæmorrhage were detected in the fundus, together with a small patch of whitish exudation. The veins bent abruptly at the edge of the cup; the retinal arteries showed a bright reflex. His doctor wrote that he had never found evidence of arteriosclerosis or high arterial tension; the urine had always been normal. Up to this date therefore there had certainly been no thrombosis of the central vein. The patient was not seen again until July, 1905, when glaucoma was present, and vision was totally lost. *The anterior chamber was deep*, T + 2. The eye had probably not been blind for more than a week. It was excised a fortnight later. Three months afterwards the patient was in good health. The left eye remained normal throughout.

Pathological Examination.

The globe is divided horizontally. The corneal surface is rough, the anterior chamber deep, the pupil slightly irregular owing to the presence of posterior synechiæ downwards and inwards. The lens is *in situ*, the vitreous free from hæmorrhage. The retina is strewn with very numerous hæmorrhages, chiefly

towards the posterior pole. The veins are very large and tortuous. The disc is cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is deeply excavated. On the side of the cup the veins are engorged, but have normal walls. Some of the arteries have also normal walls, while others are much narrowed by endarteritis. The central artery and vein are formed at about the same level in the anterior layers of the lamina cribrosa. The vein is no sooner formed than it becomes obstructed by a cellular mass (Plate IV, Fig. 1). This consists of a delicate reticulum, among which rather large cells are present with a distinct protoplasmic body and a pale nucleus. There are a few polymorpho-nuclear leucocytes, but no red corpuscles can be recognised with certainty. The vein wall is very easily seen, and is not collapsed or shrunken. The mass in the lumen has shrunk away from the wall in places, and in these situations some endothelial lining cells may be seen. They are absent, however, where the thrombus adheres to the wall. The vein wall itself, and the surrounding connective tissues, are absolutely free from inflammatory infiltration. This condition of affairs lasts throughout the whole thickness of the lamina cribrosa. Immediately beyond, it is terminated suddenly by a large collateral branch which enters at one side from the surrounding connective tissue, and restores the lumen (Plate IV, Fig. 2).

Owing to the considerable size of this twig, the vein almost immediately becomes normal again. It is filled with well-formed blood corpuscles. Farther up the nerve a slight degree of round-cell infiltration appears in the vein wall for a space, but otherwise it remains normal till the end of the series. The artery shows much endarteritis throughout its course. The whole intima, including the elastic membrane, has become detached, and lies as a collapsed mass in the centre of the lumen. This is probably an artefact. The nerve is highly atrophic. In places, the trabeculæ have become thickened, and have fallen together, giving an appearance of condensation to the nerve; in places they have retained their normal architecture, while the nerve fibres have entirely disappeared, leaving large lacunar spaces crossed by a network of supporting elements.

In the retina hæmorrhages are widespread, but usually small and confined to the internal layers. There are, however, some small subretinal hæmorrhages in the neighbourhood of the fovea. The nerve fibre, ganglion cell, and inner reticular layers are all much atrophied and œdematous; the inner nuclear to a less extent, while the outer layers are, on the whole, well preserved. At the fovea there is much distortion of the retinal elements, with loss of the pigment epithelium and adhesion to the atrophied choroid. The retinal vessels show only a moderate degree of thickening. The veins are much engorged.

The cornea is normal. The corneo-iridic angle is only very slightly occluded on the nasal side, but as far as the termination of the membrane of Descemet on the temporal. The measurements taken from the anterior end of the ciliary muscle as a convenient point are, nasally 0·22 mm., temporally, 0·76 mm. The iris stroma is condensed, cellular, and deeply pigmented. The lens measures 8·5 mm. in diameter. The ciliary body and choroid are highly atrophic. The ciliary vessels are normal.

The clinical history in this case does not give the exact date of the occurrence of thrombosis. When the patient was seen, in December, there were signs of vascular disease and a few small hæmorrhages. When seen again, in July, glaucoma had already supervened, and examination of the fundus was impossible. The macroscopical examination, however, showed the typical hæmorrhagic retinitis. From the microscopical examination it is evident that the thrombosis was of recent formation. The red corpuscles had disappeared, and the thrombus had been invaded by the endothelium. But there was as yet no proper organisation. No reaction had taken place in the surrounding connective tissues, the vein still retained its normal size and form and had not undergone the shrinkage and effacement which are found in old cases. The restoration of the lumen by the entrance of a collateral branch is exceedingly well illustrated. The marked degree of endarteritis was also a notable point.

CASE 2.—*Thrombosis of the right central vein in a patient, aged 74, suffering from arteriosclerosis and albuminuria. Glaucoma present two months later. Excision about two and a half months from onset of symptoms. Occlusion of the vein lumen by an organised cellular mass within the lamina cribrosa. Restoration of the circulation by the entrance of a large collateral branch from the trabeculæ of the nerve. Artery normal, and not much disease of the retinal vessels. Cornco iridic angle blocked only on the temporal side.*

This case was also under Mr. Lawford's care, and I am indebted to him for the clinical notes.

A gentleman, aged 74, noticed a sudden failure of the sight in the left eye in November, 1904. The urine contained albumen and the peripheral arteries were very rigid. He was seen by Mr. Beaumont, of Bath, who noted "R. retinal apoplexy with white plaques scattered about the fundus." On January 27, 1905, he was again seen, with "cyclitis and secondary glaucoma." On February 4 he consulted Mr. Lawford, who found moderate ciliary congestion, the iris discoloured and apparently swollen, the pupil small and irregular. There was no fundus reflex and the tension was + 2 fully. The eye was not very tender. It was excised on February 7, 1905. The left eye remained normal throughout. In March, 1906, his doctor reported that he was rapidly sinking from Bright's disease with anasarca and cardiac failure; there was no mention of an affection of the other eye.

Pathological Examination.

The globe is divided horizontally. *The anterior chamber is of average depth.* The corneo-iridic angle is blocked on the temporal, apparently normal on the nasal side. The lens is *in situ*. There is no vitreous or subretinal hæmorrhage. The retina is covered with numerous hæmorrhages of all shapes and sizes.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is not very deeply excavated, and the vessels on the side of the cup have normal

walls and contain blood. Immediately in front of the lamina cribrosa a normal artery and vein are formed in the usual manner. The lumen of the vein only remains free for a short distance. While still in the anterior layers of the lamina cribrosa it becomes encroached upon from one side by cellular fibrous tissue (Plate IV, Fig. 3). Organisation is well advanced in it, the stroma is distinctly fibrous, and the nuclei tend to have the elongated form of connective tissue cells. The tissue is not sharply marked off from its surroundings, and the proper wall of the vein cannot be traced with any certainty, so that it is doubtful whether it represents an encroachment from outside the wall or a cellular mass (probably proliferated endothelium) within the lumen. The appearances in subsequent sections, however, make the former more probable. At one side there is a small quantity of shrunken coagulum with a few polymorphonuclear leucocytes among it. The surrounding connective tissues are quite free from inflammatory infiltration. The obstruction is present over the whole length of the central vein within the lamina cribrosa, but is only complete over a very small area (three sections). Towards the posterior part of the lamina the vein wall is again traceable, and its lumen is filled with homogeneous coagulum in which many leucocytes, and here and there a few red corpuscles are present. A large collateral now emerges from the trabeculæ of the nerve, and plunges into this coagulum (Plate IV, Fig. 4). It carries with it a stream of normal red corpuscles, and hollows out a channel in the clot. From this point onwards the lumen of the vein is unobstructed and filled with red corpuscles. It is at first small, but soon becomes of normal size by the addition of other collateral twigs, and remains so to the end of the series. The artery is normal throughout. The nerve is considerably atrophied.

The retina shows hæmorrhages chiefly confined to the inner layers, but in places reaching as far as the outer nuclear. Most of them are small, but a few are large and have caused distortion of the retina. There are no vitreous or subretinal hæmorrhages. In general, however, the retina is well preserved except for considerable atrophy of the nerve fibre and ganglion cell layers. There is very little œdema and no coagula are found. The retinal vessels are not much diseased.

The corneo-iridic angle is practically free on the nasal side: a little blood is present in the anterior chamber and in the stroma of the iris root. On the temporal side, on the other hand, the angle is blocked nearly as far as the termination of the membrane of Descemet (0·51 mm.), and the root of the iris is somewhat atrophic. Otherwise the stroma of the iris is perfectly normal and free from infiltration. The cornea, ciliary body and choroid are normal.

The case resembles the last in its general features, but organisation is more advanced. The thrombus is limited, and the circulation is restored in the same way by the accession of a large collateral. It differs chiefly in the absence of endarteritis in the artery. The comparative slightness of the changes in the retina and in the retinal vessels is worthy of note; it is probably to be associated with the unusual freedom of the collateral circulation, and the short duration of the disease.

CASE 3.—*Thrombosis of the left central vein of* 10 *days' duration in a man, aged* 47, *the subject of gout. During the next four months increase in the retinal hæmorrhages, and finally the occurrence of a large detachment of the retina below. Urine? Glaucoma a week or two later. Enucleation six months from onset of symptoms. Central vein occupied by a fully-organised mass a short distance behind the lamina cribrosa. Lumen not fully restored in the piece of nerve excised. Widespread thrombosis with organisation of the retinal vessels. Central and retinal arteries practically normal. Corneo-iridic angle blocked on the temporal side alone.*

I am indebted to Mr. Arnold Lawson for the material and for the clinical notes.

A gentleman, aged 47, had noticed a haziness before the left eye for 10 days. V.R., 6/9; V.L., 6/36. R. fundus normal; L. thrombosis of the central vein. He had had no recent illnesses, was not anæmic, and had never suffered from syphilis. He was said to be gouty, but had never had acute gout; a few days after he was seen, however, he had a definite subacute

attack, from which convalescence was very slow. Meanwhile the eye condition showed continuous retrogression, innumerable hæmorrhages appearing in every part of the fundus. Four months after the onset of symptoms the vitreous was still clear, but a large detachment of the retina had occurred below, probably from subretinal hæmorrhage. A week or two later the eye, which up to this time had retained perception of light, was suddenly attacked by acute glaucoma. This proved intractable, and the eye was excised six months after the first onset of symptoms, having been in a state of absolute glaucoma for about a month prior to operation. The right eye remained normal throughout. The patient has not since been heard from.

Pathological Examination.

The globe is divided horizontally. *The anterior chamber is deep.* The corneo-iridic angle is not obviously occluded. The lens is *in situ.* There is a moderate amount of hæmorrhage in the vitreous. The retina is suffused in every part with large hæmorrhages, and in front of the position of the papilla there is a yellowish mass through which the retinal vessels emerge. There is a large detachment of the retina downwards and outwards. The subretinal space contains coagulum tinged with blood.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is not very deeply excavated. On the side of the cup the arteries are somewhat sclerosed, the veins are normal but small. A single central vein is formed in the anterior layers of the lamina cribrosa, and remains normal throughout its thickness. At the posterior level of the lamina it suddenly becomes occluded and replaced by a little shrunken knot of fibrous tissue (Plate IV, Fig. 5). The matrix is indefinitely fibrous, and contains many oval nuclei. The mass has shrunk away from the surrounding tissues, but the space left is not part of the original vein lumen, since it contains no blood and is not lined by endothelium. As only a very short piece of nerve was excised with the globe, the series of sections ends before restoration of the lumen has occurred. The central artery is normal throughout. The nerve is not atrophic.

The retinal vessels are much diseased, especially the veins. The change in them is usually one of thickening of their connective tissue walls, without endothelial proliferation. Many of them contain organised thrombi very similar to that found in the central vein (Plate IV, Fig. 6). They are often surrounded by pigment granules and masses which seem to have collected in the perivascular lymph spaces. These are presumably derived from the blood pigment. The retinal arteries show both endothelial proliferation and thickening of their outer coats. The retina is infiltrated and destroyed by enormous hæmorrhages, which have also broken through both into the vitreous and into the subretinal space.

The cornea is normal. The corneo-iridic angle is blocked as far as the termination of the membrane of Descemet on the temporal side (0·5 mm.); there is not much condensation or atrophy of the adherent iris root. There is a moderate round cell infiltration around the canal of Schlemm. On the nasal side the angle is quite open. A few leucocytes and pigment granules are present among the spaces of Fontana. The iris tissue generally is condensed, and there are a few small patches of round cell infiltration in its stroma and also in the anterior part of the ciliary body. The ciliary body is somewhat atrophic; the choroid is normal. The lens measures 7·5 mm. in diameter.

The thrombus in this case was somewhat more fully organised than in the last, and the vein was becoming much shrunken. The extensive thrombosis of the retinal veins was an important point. It did not affect all the veins, so that some blood was still present in the chief branches on the side of the cup. The thrombosis in the retinal veins was also not directly continuous with that in the central vein. Between the place where the vein was formed by the meeting of its main retinal branches and the site of the thrombus there was a piece of vein with a clear lumen and more or less normal walls. The thrombi in the retinal vessels were therefore not formed directly by spreading of the process from the thrombus in the central vein, but were formed independently, presumably as a result of the

interference with the circulation. In spite of the definite history of gout, there was no evidence of inflammatory infiltration of the vein wall apart from the site of the thrombus.

CASE 4.—*Thrombosis of the left central vein of 10 days duration. T. slightly +. Anterior chamber of normal depth. Trace of albumen in the urine on one occasion only. Definite onset of glaucoma two months later. No improvement in spite of eserin and iridectomy. Excision four months from onset of symptoms. Occlusion and almost complete effacement of the central vein in the anterior part of the lamina cribrosa by a cellular organised mass. Extensive endarteritis. Retinal vessels much diseased. Corneo-iridic angle occluded equally on the two sides.*

I am indebted to Mr. Fisher for the use of the following clinical notes :—

A man, aged 60, came to the Royal London Ophthalmic Hospital on November 15, 1905, complaining of a mist before the left eye of 10 days duration. V.R. 6/6 with + 1·25 D sph. V.L. fingers at 20 cm. The left pupil reacted only slightly to light. The anterior chamber was of normal depth. The ophthalmoscope showed "thrombotic retinitis" with silver wire arteries. The tension was slightly raised. The urine on this occasion showed a slight trace of albumen, but this could not be detected on several subsequent examinations, and the specific gravity was usually about 1020; there was no glycosuria. Ten days later the retinal hæmorrhages were still more extensive. On January 24, 1906, he presented himself with a definite attack of glaucoma. The tension was + 2 or + 3, the cornea hazy, the pupil semidilated and fixed. *The anterior chamber was deep and remained so.* In spite of the use of eserin, etc., the tension remained high and an iridectomy was therefore performed on February 27. It was followed by much hæmorrhage from the iris and conjunctiva and no lowering of the tension was obtained. The eye was therefore excised on March 10, 1906. The right eye remained normal throughout.

Pathological Examination.

The globe is divided horizontally. The iridectomy wound is bulging. The pillars of the coloboma are free. The anterior chamber is deep and contains blood. The corneo-iridic angles seem to be occluded. The lens is large and is in contact with the ciliary processes all round its equator. The vitreous is clear. The retina is *in situ* and is strewn with innumerable streaky hæmorrhages, especially round the papilla. In the macular region there are many white spots, but no recent hæmorrhages. The retinal vessels are barely visible. The disc is cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—In the retina, in the neighbourhood of the papilla, the vessels show very great changes, especially the arteries. There is both endarteritis and thickening of the outer coats, the latter being often the seat of true hyalin degeneration, with loss of nuclear staining. Some of the vessels are completely occluded by these processes; the veins are enlarged and full of blood. Their walls are often much thickened and sometimes show localised round-cell infiltrations. There is no endothelial proliferation.

The branches of the central vein unite into a common trunk immediately in front of the lamina cribrosa. This is no sooner formed than it becomes collapsed and blocked by a shrunken cellular mass. The ground substance is homogeneous; the cells are oval or elongated. There are no red corpuscles or polymorphonuclear leucocytes. Towards the posterior part of the lamina the shrinkage becomes less extreme, a few red corpuscles and leucocytes are visible in the homogeneous mass, and at the same time a distinct round-cell infiltration appears in the surrounding connective tissue (Plate V, fig. 7). The vein lumen then becomes free once more and has a normal endothelial lining, but it is still very small, while the walls are thick and somewhat infiltrated. The lumen speedily enlarges, while the infiltration becomes less. Some distance up the nerve there are two small areas of endothelial proliferation, but they do not materially narrow the lumen, and are only present for a very short distance. The lumen remains patent, and filled with blood as far as the end of the series.

The artery in its whole course behind the lamina is extensively diseased, especially posteriorly. The changes are entirely within the lamina elastica. Next to this membrane comes a layer four or five deep of large, pale, blown-out cells, usually with eccentric nuclei. The limits between cell and cell are fairly clear; the protoplasm is very faintly stained and slightly granular. Within this there is a layer of dense laminated tissue with nuclei elongated transversely. The lumen is narrow, filled with blood, and situated quite eccentrically. Its endothelium is well preserved. Elastic staining shows the presence of fine fibres among the dense tissue immediately beneath the endothelium, but not among the blown-out cells. It seems probable that these cells are not derived from the endothelium, which forms an unaltered layer lining the lumen, but from the subendothelial tissue normally present between the endothelium and the elastic lamina. The papilla is deeply cupped and the nerve is atrophied and shrunken.

Hæmorrhages in the retina are less abundant than usual. They are probably becoming absorbed, as large areas are found where the retinal tissues are destroyed, although there are only a few red corpuscles. As usual, the outer layers—rods and cones, and outer nuclear—are much the best preserved; the inner are almost totally destroyed towards the posterior pole, better preserved in the periphery. The retinal vessels show the same changes as have already been described on the papilla.

The corneal epithelium is œdematous, the stroma normal. The corneo-iridic angle is occluded on both sides to a point a little beyond the termination of the membrane of Descemet. The occlusion is equal on the two sides (about 0·77 mm.). There is evidence of considerable old iritis. A thin fibrous membrane stretches across the pupil. There is a layer of new-formed fibrous tissue on the front of the iris, which has caused ectropium uveæ by its contraction. Among this tissue and in the angle of the anterior chamber there are a few blood corpuscles. The iris stroma is much condensed and deeply pigmented. The ciliary body is atrophic. There is much sclerosis of the choroidal vessels, especially the arteries. The ciliary arteries also, both anterior and posterior, show endarteritis. The lens measures 8 mm. in diameter.

The case is an example of the commonest type of pathological lesion, a thrombus fully organised, and causing total obliteration and almost complete disappearance of the vein. The slight cellular infiltration of the walls of some of the retinal vessels may be associated with the inflammatory reaction in the anterior part of the eye due to the iridectomy. The case also furnishes a good example of the association of advanced endarteritis with thrombosis of the vein. Glaucomatous changes at the corneo-iridic angle and in the papilla were marked.

CASE 5.—*Thrombosis of the left central vein in a woman aged* 60. *Much cardiac hypertrophy and general arteriosclerosis; no albuminuria. Eight to ten months later glaucoma. Enucleation* 12½ *months from onset of symptoms. Slight contraction of field of vision, and lens opacities in right; no retinal hæmorrhages. Total obliteration of the central vein in the region of the lamina cribrosa by a cellular organised thrombus. Gradual restoration of the lumen by the accession of small collateral twigs. Advanced endarteritis in the central artery. Retinal vessels much diseased. Corneo-iridic angle more occluded on the temporal than on the nasal side.*

I have to thank Mr. Lang for permission to use the clinical notes of this case.

A woman, aged 60, came to the Royal London Ophthalmic Hospital on May 19, 1904, complaining of dimness of vision of the left eye. A diagnosis of thrombosis of the left central vein was made. V.R. with −4 D sph. = 6/9; V.L. = 6/18 not improved. There were slight lens opacities in both eyes, but the right fundus was normal. There was marked general arteriosclerosis and cardiac hypertrophy, but no albuminuria. Ten months later she returned with glaucoma of the left eye, the cornea hazy, the pupil dilated and fixed, the tension + 2. The eye had been painful for two months. It remained glaucomatous in spite of treatment, and as vision was totally lost, it was enucleated on June 3, 1905. A slight contraction of the field of vision was noted in the right eye in May, 1905, otherwise it remained normal throughout.

Pathological Examination.

The globe is divided horizontally. The cornea is clear, *the anterior chamber of normal depth.* The iris pattern is not obscured, the corneo-iridic angles appear to be occluded. The vitreous is free from hæmorrhage. The retina is *in situ*, and shows a moderate number of hæmorrhages, especially in the temporal periphery. The disc is deeply cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—There is deep glaucomatous cupping. On the side of the excavation the vessels, both arteries and veins, are exceedingly small and thick walled. The arteries especially are narrowed almost to obliteration by endarteritis and thickening of the middle coat. The main artery is formed at the bottom of the cup, the vein somewhat farther back in the anterior layers of the lamina cribrosa. Almost immediately it becomes occluded. The obstruction consists of a finely fibrillar tissue with a number of rather large oval nuclei in it, together with a few red corpuscles and polymorphonuclear leucocytes (Plate V, Fig. 8). It is difficult to say whether the oval cells are derived from the endothelium or from the surrounding connective tissue cells. The former seems more probable, since the cellular knot is entirely within an area of the normal size of the vein lumen, and there is absolutely no cellular infiltration of the surrounding connective tissues. The lumen of the vein is completely filled; there is only a small cleft at one side, which is probably artificial, since it is not lined with endothelium. In the succeeding sections red blood corpuscles entirely disappear from the tissue, and it becomes much denser and less cellular, a few polymorphonuclear leucocytes still remaining, however. The nodule still completely fills the vein. The tissue now becomes much more cellular again, the nuclei being more like those of ordinary connective tissue. The ground substance is also more definitely fibrous. The shape and appearance of a vein is entirely lost, there is no trace of a lumen or vein wall, merely a little cellular knot without definite boundaries in the position which it ought to occupy (Plate V, Fig. 9). The connective tissue around the vessel remains free from all infiltra-

tion except in this position. This condition remains for a very considerable distance. Finally, however, a minute branch from the surrounding tissues plunges into the knot, and taking up a central position in it, restores a minute blood filled and endothelium lined lumen in the normal position of the vein (Plate V, Fig. 10). Very gradually other similar collaterals are added, but even up to the last sections of the series the lumen is by no means restored to its original size, while the wall of the vein remains very thick, and shows a considerable infiltration of round cells. The surrounding connective tissue remains quite free from round cell infiltration.

Throughout its whole course in the nerve the artery shows a very marked and somewhat peculiar endarteritis (Plate V, Figs. 8, 9, 10). It represents a more advanced condition of the condition shown in Fig. 11 of my former paper. There is a small and very eccentrically placed lumen. This is lined by a single layer of apparently normal endothelial cells. Between these and the elastic lamina there is a thick layer of cells, with large somewhat pale nuclei and swollen vacuolated bodies. Some of them are very large, contain many nuclei, and have all the appearance of small giant cells (Plate V, Fig. 10). Giant cells have been described in endarteritis by v. Michel.* Close to the endothelium the cells are less swollen, and their nuclei tend rather to be elongated. These cells show a great tendency to break down, so that between the endothelium and the elastica there is often simply a space filled with granular detritus. There are a few short elastic fibres among the cells, but they also have largely broken down. In places the elastica itself has become detached, but this is probably an artefact.

The nerve is very atrophic; practically no fibres remaining. In parts the trabeculæ have fallen together, so that the nerve is much condensed; in parts this has not occurred, and empty spaces are left, crossed only by the neuroglial supporting structures.

In the retina the veins show a very considerable thickening of their connective tissue walls, without endothelial proliferation. The lumen is concentrically narrowed. In places the nuclear staining is very imperfect, and there is probably true hyaline

* Zeitsch. f. Augenh., vol. ii, p. 1, 1899, Plate I, Fig. 2.

degeneration. The walls of the arteries are also thickened, but not so much so as in the case of the veins. There is no endothelial proliferation. The retina shows comparatively few hæmorrhages. Its inner layers—nerve fibre, ganglion cell, inner reticular and inner nuclear—are much atrophied, its outer well preserved. There are no subretinal or vitreous hæmorrhages The cornea is normal, the iris and ciliary body are much condensed and atrophic; there is slight ectropium uveæ. The corneo-iridic angle is occluded on both sides, but considerably more on the temporal (1·31 mm. as against 0·85 mm). There is some vascular disease of the choroid, but no imflammation. The lens measures 8·5 mm. in diameter.

The case shows in a typical manner all the lesions most commonly found in cases of thrombosis of the central vein. The mass occupying the vein lumen within the lamina was no doubt a portion of the original thrombus not yet fully organised. Then follows a considerable area in which organisation is very advanced, and has caused obliteration and almost complete disappearance of the vessel. Finally the lumen is gradually restored by the accession of small collaterals from the trabeculæ and surrounding connective tissue, but the wall remains thick and infiltrated for a space. The advanced state of organisation is to be associated with the long duration of the case.

Case 6.—*Thrombosis of the left central vein in a man aged* 31. *Onset probably during an attack of influenza a fortnight before. History of syphilis. Glaucoma already present when first seen, and fundus invisible. No improvement with eserin and paracentesis. Enucleation about four to six months from the onset of symtoms. Marked inflammatory infiltration of the central and all the retinal veins. Complete obliteration of the central vein for a short distance within the lamina cribrosa. Central artery normal throughout, except for slight infiltration of its walls. Root of the iris widely adherent to cornea. Extreme condensation of iris and ectropium uveæ.*

I am indebted to Mr. Holmes Spicer for the use of the following notes:—

A man, aged 31, came to the Royal London Ophthalmic Hospital on November 10, 1905, complaining of dimness of vision in the left eye. He was uncertain as to its duration, but vision had been quite good in this eye 3 to 5 months before. It had failed especially within the last fortnight, after an attack of influenza. The eye had been painful for three days. Two and a-half years before, he had had a chancre. Six months later he had "rheumatism" of the knees, ankles, and elbows. The left eye at that time was red and watery, and the lids were swollen (?syphilitic iritis). V.R. 6/5. Eye normal in every respect. V.L. fingers at 6 in. Projection good. There was considerable lacrymation and photophobia, with ciliary and conjunctival congestion. The cornea was slightly hazy, and there were some fine precipitates on the back of it. *The anterior chamber was deep.* The pupil was regular and dilated to an extreme degree, only a narrow rim of iris about 1 mm. wide being visible. The iris was dull and new vessels were present on its surface. There were many large opacities in the vitreous, so that although a good red reflex was obtainable in all directions, no details of the fundus could be observed. The tension was + 1. A provisional diagnosis of cyclitis was made.

Treatment with eserin, etc., had no effect in reducing the tension or contracting the pupil, and a paracentesis was therefore performed on November 31. This also was without effect on the tension, and was followed by a large hyphæma. The eye remained painful, and was therefore excised on December 1. The right eye remained normal throughout.

Pathological Examination.

The globe is divided sagittally. The cornea is hazy, the anterior chamber deep. The iris is very short, adherent to the back of the cornea over most of its extent. There is marked ectropium uveæ. The lens measures 9·5 mm. in diameter. The vitreous contains a considerable amount of blood. The retina is strewn with numerous small punctiform hæmorrhages. The veins are large but not very tortuous. The disc is cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is moderately deeply excavated. On the side of the cup the veins are greatly engorged and show a very marked infiltration of their walls, with round cells. They are not thickened. The arteries are normal. At the level of the bottom of the cup, and while still in front of the lamina cribrosa, the vein suddenly becomes collapsed, and its lumen, previously distended with normal red blood corpuscles, contains a small quantity of shrunken homogeneous coagulum, which adheres to the wall at one side. The round-cell infiltration of the wall is considerable, and encroaches a little on the lumen. The surrounding connective tissues are also infiltrated. In the next sections the encroachment on the lumen becomes complete, so that it ceases to be traceable. For a short space the position of the vein is quite indistinguishable. Soon, however, it reappears again in the same position relative to the artery as before. A conical mass of organised tissue projects into its lumen, leaving only a little cleft at one side, which is filled with homogeneous coagulum similar to that found on the other side of the obstruction (Plate V, Fig. 11). The lumen quickly increases at the expense of the conical mass, and very soon reattains its normal size. All these changes are completed before the vein emerges from the posterior surface of the lamina. The cause of the restoration is not evident in this case; no considerable collateral vessel can be seen to enter the vein. Until the end of the series the vein remains of normal calibre. The wall is throughout moderately infiltrated with round cells, but is unthickened. The artery is normal in its whole course. The nerve is only slightly atrophied.

The retinal vessels show very advanced changes. All the large veins are surrounded by a thick layer of round-cell infiltration. This is not merely in the perivascular lymph sheaths but also in the vein wall itself (Plate V, Fig. 12). The lumen is considerably invaded. In places also there are organised thrombi within the veins, but these are generally of limited extent. These various processes not infrequently cause total obliteration of the vessels, in other places again they are much distended. The arteries also show some infiltration of their walls and proliferation of their endothelium, but to a very

much smaller extent than the veins. They are usually empty. There is a slight general infiltration of the inner layers of the retina, and some small patches of choroido-retinitis are present about the equator. The nerve fibre and ganglion cell layers, especially the latter, are somewhat atrophic; the outer layers are œdematous, but on the whole well preserved. In the retina itself hæmorrhages are comparatively small and scanty, but they are abundant in the vitreous. Many blood corpuscles lie on the anterior surface of the retina, and among them there are delicate fibres with elongated nuclei upon them. These often form thin membranes of considerable extent, fused with the retina in places, but in others separated from the limitans interna by a distinct space. They are sometimes supplied with small twigs from the retinal vessels. They undoubtedly represent commencing organisation of the blood in the vitreous—an early stage of retinitis proliferans.

The iris stroma is condensed and cellular. The root of the iris is adherent to the back of the cornea equally above and below; the adhesion extends beyond the termination of the membrane of Descemet, and the root of the iris is atrophic. There is marked ectropium uveæ, caused by the contraction of a new-formed fibrous layer on the front of the iris. The sphincter pupillæ has also a sharp forward kink near its inner end. There is blood in the anterior chamber. The fibrous tissue on the front of the iris closely resembles that on the anterior surface of the retina, and has probably been formed in the same way—by the organisation of blood extravasations. The cornea is normal, the ciliary body and choroid are atrophic, but free from infiltration. The lens has dropped out of the sections.

The case shows a quite unusual degree of inflammation, which is mostly confined to the walls of the vessels, especially the veins. It is evident that these are not the ordinary processes of angiosclerosis—that some toxic agent has probably been circulating in the vessels. According to the clinical history this was probably the toxine of influenza. I have already pointed out that a history of influenza is comparatively frequent in cases of thrombosis, especially in

those occurring in young subjects who do not show signs of arteriosclerosis. The occurrence of retinitis proliferans is also very possibly to be associated with a toxic condition of the blood, since, as Flemming has shown, that disease, although associated with hæmorrhage, probably also requires a circulating toxine for its production. Harms mentions the occurrence of influenza in two of his cases (Cases 3 and 9), and one of these was aged 20.

The changes in the iris most probably dated, in part at least, from the eye trouble which followed the syphilis two years before. They were much too advanced to coincide with the comparatively short history which he gave of his present attack. The extreme dilatation of the pupil, which was the most remarkable point in the clinical history, was due partly to the ectropium uveæ seen through a hazy cornea, partly to the shortening of the iris by the contraction of the new-formed fibrous tissue on its anterior surface.

CASE 7.—*Thrombosis of the left central vein in a woman aged* 30, *probably of three months' duration. Onset of glaucoma shortly after first visit. No improvement with eserin and paracentesis. Excision about four months from commencement of symptoms. Obliteration of vein, with imperfect canalisation in the posterior layers of the lamina cribrosa. Round-cell infiltration of connective tissue around retinal and central veins. Corneo-iridic angle equally occluded on the two sides.*

I am indebted to Mr. Lang for the use of the case.

A woman, aged 30, came to the Royal London Ophthalmic Hospital on December 8, 1904, complaining of failure of vision in the left eye, of three months' duration. V.R. 6/6. V.L. perception of light. The opthalmoscope showed typical thrombosis of the central vein in the left. There was no evidence of syphilis. She had suffered from bilious attacks, with vomiting and headache, within the previous two to three years. The urine contained a trace of albumin and a few granular casts. She returned in three weeks, complaining of pain in the left eye. It was glaucomatous, the pupil semidilated and fixed, the anterior

chamber rather shallow. There was moderate circumcorneal congestion, a small hyphæma, and the tension was +1. Perception of light was completely lost. The disc of the right eye had somewhat blurred edges, but vision was still 6/6, the field full, and the tension normal. Eserin was used and a paracentesis performed, but without any good result, and as the eye remained painful, it was excised on January 8, 1905. In March, 1905, according to a communication from her husband, she was in good health and her other eye was unaffected.

Pathological Examination.

The globe is divided horizontally. *The anterior chamber is of average depth.* The lens is *in situ.* The vitreous contains exudation and a little hæmorrhage. A whitish-yellow mass lies over the position of the disc. There are very numerous hæmorrhages, especially in the neighbourhood of the disc, on the nasal side; somewhat fewer temporally. A large subretinal hæmorrhage is present below.

Microscopical Examination—

Optic Nerve and Central Vessels.—The disc is only moderately excavated. Within the cup, and in the vitreous in front of it, there is a quantity of hæmorrhage and coagulum. This is becoming invaded by fine vascular connective tissue, which springs from the lining tissue of the cup. The veins on the side of the cup are much thickened, the lumen being narrowed in a concentric manner. There is slight round-cell infiltration around their walls, but the thickening itself, which affects the fibrous tissue of the wall, is not unduly cellular. The endothelium is not proliferated. The arteries are normal.

At the bottom of the cup a single artery is first formed, and a few sections farther back the vein appears. There is a very distinct round-cell infiltration of the connective tissues around the vessels. Both contain blood. Some small hæmorrhages are present in the substance of the nerve at this level. Towards the posterior surface of the lamina the vein very suddenly becomes obliterated. Its situation is marked by an area of round-cell infiltration, among which a few blood corpuscles are present. There is however no lumen, and its wall cannot be traced. The cellular infiltration has no definite outer boundary, but is

lost gradually in the surrounding connective tissues. The artery at the same point shows for the first time some vacuolation and proliferation of its endothelium. A few sections farther back three small lumina appear within the little cellular knot (Plate VI, Fig. 13). Each is lined with endothelium and contains homogeneous coagulum, with here and there a few red blood corpuscles. So far as can be determined, they do not arise by the entrance of vessels from without, but represent channels formed *in situ* from the proper venous lumen beyond. They represent therefore an incomplete stage in a process of canalisation. Following the vein up the nerve, a single lumen is speedily reformed. It remains small, and the wall of the vein is infiltrated for some distance, but with the entrance of several accessory branches the lumen slowly enlarges, while at the same time the infiltration gradually subsides, so that before the end of the series the wall is again normal. Over the area of greatest change in the vein the artery shows a moderate degree of endarteritis, but this also disappears again farther up the nerve. The nerve itself is much atrophied.

The retinal vessels show changes similar to those already described on the side of the cup. Hæmorrhages are extremely abundant in and beneath the retina, and also in the vitreous. The retina is much distorted by them, and there are large coagula in the internuclear layer. Over the whole of the posterior part of the retina there is a comparatively thick layer of connective tissue. It is dense and cellular on its inner side, somewhat looser externally, and its vessels are numerous but small. Over a large part of its extent it has no connection with the retina, and it is intimately connected with it only at the papilla. In the periphery it ends in fine threads, which sometimes become attached to the surface of the retina and sometimes disappear among the vitreous hæmorrhages. Probably by its contraction the retina has been thrown into a number of folds, and the limitans interna shows many much finer crenations. The case furnishes, in short, a good example of retinitis proliferans.

With regard to changes in the anterior part of the eye, the cornea is normal. The stroma of the iris is atrophic and condensed. There is a thin layer of new-formed fibrous tissue on its

anterior surface, which has caused ectropium uveæ with anterior kinking of the sphincter. The angle of the anterior chamber is shut off by adhesion of the root of the iris about equally on the two sides (0·85 mm.). The ciliary body is atrophic and the choroid is normal. The lens measures 8·25 mm. in diameter. There are no signs anywhere of recent inflammation.

The resemblance between this case and Case 6 reported above should be noted. In both the patient was unusually young (31, 30), the ordinary changes of angiosclerosis were conspicuously absent, while, on the other hand, there was considerable inflammation of the vein walls. At the site of obstruction also the signs of inflammation were unusually prominent. In both there was retinitis proliferans, and in both there was probably a toxic condition of the blood (influenza, and perhaps syphilis in Case 6, albuminuria in Case 7). In both there was new-formed fibrous tissue on the front of iris, with ectropium uveæ. They show therefore a coincidence on a number of more or less unusual points, which seems to indicate that they should be classed together, and somewhat apart from the others. I shall discuss this later.

In the present instance also the obstructed area was unusually small; it occupied only some six sections. The case furnishes a good example of an early and incomplete stage of canalisation, which is an unusual condition in thrombosis of the central vein. I have described and figured a more advanced stage of the same condition in Case 2 of my former paper, and a similar condition has since been reported by Sidler-Huguenin, and by Harms.

Case 8.—*Failure of sight in a man, aged* 61, *the subject of arteriosclerosis. Onset of glaucoma six weeks later. Iridectomy followed by expulsive hæmorrhage. Enucleation. Organised thrombus in the vein in the posterior layers of the lamina cribrosa.*

I am indebted to Mr. Percy Flemming for the material and notes.

A man, aged 61, came to University College Hospital with symptoms of glaucoma in his left eye. He gave a history of failure of sight in that eye for six weeks before it became painful. The tension was +2 and all the signs of glaucoma were present. Vision was reduced to perception of light in the temporal field only. The peripheral arteries were rigid and there was cardiac hypertrophy. The urine contained no albumen or sugar. The fundus was invisible, but, in view of the history, hæmorrhagic retinitis was suspected. As the glaucoma did not prove amenable to treatment, an iridectomy was performed. This was followed by expulsive hæmorrhage, and the eye was enucleated.

Pathological Examination.

The globe is divided sagittally. The corneal wound is laid back in the form of a flap, and the intraocular contents are prolapsed into it. The eye is full of blood clot, and the intraocular structures are barely distinguishable.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla shows a moderately deep glaucomatous cup, which is filled with hæmorrhage. The veins on its side are much engorged, and their walls are considerably infiltrated with polymorpho-nuclear leucocytes. This infiltration, however, does not extend beyond the lamina, and is probably a sign of commencing infection of the eye due to tearing open of the wound by the intraocular hæmorrhage. The arteries are infiltrated as well as the veins; they are well filled with blood and show no endarteritis. Towards the posterior part of the lamina cribrosa the vein suddenly becomes very small, and its lumen contains some shrunken homogeneous coagulum pressed up against one wall, as well as some red corpuscles. Presently the whole lumen becomes filled with the clot, all formed red corpuscles having disappeared. The coagulum at the same time becomes more fibrillar, with little spaces and clefts among the fibrils. It becomes invaded by spindle-shaped cells with elongated nuclei (Plate VI, Fig. 14). There is no round-cell infiltration of the surrounding connective tissues, and the outline of the vein is not entirely lost. This condition lasts for a considerable distance above the lamina cribrosa; then a small

vessel finds its way into the cellular knot, and a little empty lumen is restored. It speedily enlarges by the entrance of collaterals, but does not regain its normal size for some distance. The wall is not at all thickened and the vessel remains empty and collapsed, but without inflammatory infiltration of its wall.

Over the whole area in which the vein is obstructed the artery is normal and distended with blood. Higher up the nerve, however, its lumen becomes very considerably narrowed by endarteritis, which gradually increases in ascending the nerve, so that in the last sections only a very small and eccentric lumen remains. The nerve is very highly atrophic, in places much condensed, in places loose in structure and œdematous.

The intraocular hæmorrhage is chiefly sub-retinal, partly also sub-choroidal and in the vitreous. The lens and most of the vitreous have been expelled. The retina, iris and ciliary processes are prolapsed into the wound. There are many hæmorrhages in the substance of the retina; the retinal vessels show infiltration of their walls with polymorphonuclear leucocytes, but no angiosclerotic changes. The iris stroma contains abundant hæmorrhage. The ciliary vessels are normal, and the choroidal do not show much sclerosis.

The association of thrombosis of the central vein with expulsive hæmorrhage does not seem to have been observed before. Possibly this is because the central vein is not usually examined in these cases. I do not believe, however, that thrombosis of the vein is a common cause of expulsive hæmorrhage. In the first place, so far as the records at my disposal go, it would seem that when iridectomy is performed upon such eyes, and when the eye is subsequently lost, the loss is not usually due to expulsive hæmorrhage, but to return of the glaucoma with gaping of the wound, etc. Again, in almost all cases of expulsive hæmorrhage the effusion is sub-choroidal, not retinal, sub-retinal or intravitreous, as might be expected if it were due to a block on the central vein. Naturally, however, if there were an obstruction of the vein, one would expect the retinal vessels to add their quota to the hæmorrhage, as they evidently did in the present instance.

CASE 9.—*Gradual loss of vision in the left eye during* 16 *months, then sudden and complete failure. Ophthalmoscopically, thrombosis of the central vein. T. n. in both. One month later left glaucoma. Enucleation about* 18½ *months from onset of symptoms. Great narrowing of the vein behind the lamina, apparently from endothelial proliferation. Capillary channel still present. Retinal arteries and veins much diseased. Corneo-iridic angle more occluded on the temporal than on the nasal side.*

I am indebted to Mr. Lang for the use of this case.

A man, aged 58, came to the Royal London Ophthalmic Hospital on December 4, 1905, complaining of gradual failure of the vision of the left eye of 16 months' duration. Vision had then failed suddenly and completely. When seen five days later the typical picture of thrombosis of the central vein was present. The tension was normal in both eyes. V.R. 6/6; fundus normal. V.L. Perception of light. The urine contained no albumen or sugar. About 2½ months later he reappeared with symptoms of glaucoma in the left eye, dusky pericorneal congestion, hazy cornea, slightly shallow anterior chamber, pupil moderately dilated, T + 1. The eye remained painful in spite of treatment, and was therefore excised a week later.

Pathological Examination.

The eye is divided horizontally. The cornea is hazy, *the anterior chamber fairly deep.* The iris markings are very clear. The corneo-iridic angle seems to be occluded for a short distance. The lens is large, and almost fills the interciliary space. The vitreous contains a few flocculi of exudation, no hæmorrhages. The retina is *in situ*, and is infiltrated in every part with large hæmorrhages. The vessels are invisible. The disc is not cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—In front of the lamina cribrosa there is a considerable endarteritis in the main branches of the artery. The veins are also thick walled. They are distended with blood. In the anterior part of the lamina a round-cell

infiltration appears at one side of the vein. The vessel contains homogeneous coagulum, with only here and there a red blood corpuscle. At the same time the endothelium thickens greatly, forming a layer several cells thick. The intima has partially shrunk away from the connective tissue wall, probably artificially. The round-cell infiltration soon ceases, but the thickening of the intima progresses gradually, so that a short distance behind the posterior level of the lamina the lumen is reduced almost to capillary dimensions (Plate VI, Fig. 15). It measures 8μ instead of 120μ to 140μ. The obstruction does not seem to have been absolutely complete, however; a minute stream was probably present during life. The tissue obstructing the vein is not of the usual type, it has a definite concentric lamination, and contains elongated nuclei, which also have a concentric arrangement. It encroaches on the lumen from all sides, but leaves a central free portion containing blood. Altogether the appearance is more suggestive of proliferation of the endothelium (endophlebitis) than of organisation of a thrombus. Weigert's elastic tissue stain shows no elastic fibres among the proliferated cells. The disease of the vein wall ceases rather suddenly; the thickening of the intima is no longer present all round, but becomes confined to a bud-like excrescence on one wall. This shortly disappears, leaving a somewhat small, but otherwise normal vein. The vessel soon enlarges, by the accession of large trabecular branches, and remains of full size till the end of the series. The artery is normal throughout. The nerve is only slightly atrophic, solitary loculi being often singled out.

The retinal veins are much diseased, especially those of large and medium size. The lesion seems to be a combination of thickening of the connective tissue wall and endothelial proliferation. There is no evidence of thrombosis in any of the retinal vessels. The arteries are also thick walled, but are much less diseased than the veins; there is no endothelial proliferation. The retinal hæmorrhages are in general small but diffuse, so that while no considerable part of the retina is free, the retinal layers are usually well preserved. In the neighbourhood of the macula, however, there are some very large hæmorrhages, with large blood-filled spaces between the nuclear layers, and destruction of the retinal tissue.

The disc is not cupped, and the nerve is atrophic only in patches, which probably corresponded to portions of the retina destroyed by hæmorrhage.

The cornea is normal. The angle of the anterior chamber is occluded for a short distance on both sides, but decidedly more on the temporal; the measurements are, nasal 0·342 mm., temporal 0·461 mm. The iris stroma, ciliary body and choroid are perfectly normal and free from infiltration. The transverse diameter of the lens measures 8 mm.

This case seems to furnish an example of obstruction of the central vein brought about not by the formation of a thrombus within it, but entirely by narrowing of the lumen owing to disease of the wall. There was evidence that a minute and quite insufficient blood stream had been present throughout the whole course of the disease. A gradually increasing disease of the vein wall would accord well with the somewhat unusual history of a gradual loss of vision during sixteen months. The sudden loss of sight two months before he was seen probably corresponds to the occurrence of the specially large hæmorrhages found in the macular region.

The case shows well the early stage of glaucoma following thrombosis. Glaucoma had probably lasted some 12 to 14 days when the eye was excised. Inflammatory infiltration was entirely absent from the iris stroma or root. The iris was adherent, but only loosely and for a short distance. There was no atrophy or condensation of the tissue. As is extremely common in these early cases, the adhesion was more extensive on the temporal side.

Case 10.—*Ophthalmoscopic appearances resembling those of thrombosis of the left central vein, except that both the veins and arteries were extremely small. Duration doubtful. Three months later, glaucoma. Excision about a month from onset of glaucoma. Organised thrombus in vein within lamina cribrosa. Complete obliteration of artery in anterior layers of lamina by a nodule of endarteritis. Extensive thrombosis of*

retinal veins. Occlusion of corneo-iridic angle greater on the temporal side.

I am indebted to Mr. H. Parker for the material and clinical notes of this case, and to Mr. W. I. Hancock for obtaining them for me.

A woman, aged 34, came to the Central London Ophthalmic Hospital on December 29, 1904, complaining of loss of vision of the left eye. The opthalmoscope showed numerous large hæmorrhages all over the fundus. The disc was white, and both arteries and veins were barely visible. The pupil was inactive to light and the tension was normal. The right eye was normal; V. with −0·75 sph. 6/6. She had suffered from joint pains at intervals since she was 15 years of age, but there was no history of rheumatic fever. The heart, lungs, and urine were normal. On March 30, 1905, she reappeared, with glaucoma of the left eye of three days' duration. T. + 1½. There were no signs of iritis and no cupping of the disc. Eserine produced no improvement, and the eye was therefore enucleated about a month after the onset of glaucoma.

Pathological Examination.

The globe was preserved in Müller's fluid. It was divided horizontally. The depth of the anterior chamber is not noted. The aqueous and vitreous contain coagulated exudation but no blood. The angle of the anterior chamber appears to be occluded. The lens is *in situ*. The retina is *in situ*, and is strewn in every part with hæmorrhages.

Microscopical Examination—

Optic Nerve and Central Vessels.—The papilla is excavated. The cup is filled with a coagulated exudation, and there is also a quantity of delicate new-formed fibrous tissue (retinitis proliferans). It partially clothes the sides, and fills in the bottom of the cup. It consists of a delicate meshwork of fibres with elongated nuclei. At one spot, however, the tissue is denser, and is occupied by a large number of small convoluted blood vessels. These are supplied by vessels which arise from small twigs, probable veins, in the substance of the papilla.

The vessels on the side of the cup are small, and for the most part empty. Their walls show much thickening of the "fibrosis" type, with concentric narrowing of the lumen. The endothelium is not proliferated. The description applies to both arteries and veins.

Towards the bottom of the cup the lumen of the artery becomes very small and collapsed, and in the superficial layers of the lamina it is completely obliterated by endarteritis (Plate VI, Fig. 16). The muscular coat is intact; among the proliferated cells small curly elastic fibres are visible. The obstruction lasts for only a short distance; while the vessel is still within the lamina the endarteritis gives place to homogeneous coagulum, and before long red blood corpuscles are again found. The artery soon becomes free from endarteritis, and remains so till the end of the series.

The vein commences to be obstructed as soon as it is formed. At first its lumen is very wide, and contains granular *débris*, among which pale elongated nuclei of endothelial cells and a few delicate fibrils are visible (Plate VI, Fig. 16). Gradually the cells become more numerous and the fibrils more distinct, forming a close meshwork. The connective tissue wall of the vein also seems to take part, the cells contributed by it being smaller, rounder, and more deeply stained than those contributed by the endothelium. In places a group of cells of the endothelial type is found in the centre, surrounded by a ring of cells of the connective tissue type. Finally the tissue becomes denser and less cellular (Plate VII, Fig. 17). The obstruction occupies a very considerable length of the vein, much greater than in the case of the artery. It ends rather abruptly in a bluntly conical process at the point of entrance of a minute collateral branch. This occurs only in the last few sections of the series, so that the state of the vein wall beyond the seat of obstruction cannot be described with certainty. The nerve is very atrophic and condensed.

The retinal veins show extremely advanced changes, evidently due to the organisation of thrombi within them. In places they are represented merely by little shrunken knots of cellular tissue; in places one, or sometimes several, small lumina are present, probably the result of canalisation. In many places there are

collections of brown pigment granules around the veins. The arteries are collapsed and thick walled, but do not show much endothelial proliferation.

The retinal hæmorrhages have for the most part been absorbed, but the retina is extremely degenerated. The nerve fibre, ganglion cell, and inner reticular layers have disappeared altogether, only the supporting framework remaining, with many œdematous spaces in its meshes. The inner nuclear layer is reduced to a few scattered cells. Between it and the outer nuclear layer there are large spaces often containing coagula. The outer nuclear layer is on the whole well preserved, but where the changes are most advanced it shares in them. The rods and cones are fairly well preserved. There is sub-retinal and vitreous coagulum, but no recent hæmorrhage in either situation.

The cornea is normal. The anterior chamber is filled with coagulum. The iris shows extreme condensation of its stroma. There is a layer of new-formed connective tissue on its anterior surface, which, by its contraction, has greatly diminished the breadth of the iris, and has pulled the sphincter, and with it the uveal pigment, round anteriorly. There is a firm adhesion of the root of the iris to the back of the cornea. On the nasal side it measures 0·93 mm., on the temporal 1·71 mm. On the temporal side the iris is adherent in its whole breadth. The ciliary body and choroid are highly atrophic.

The case was a puzzling one clinically, inasmuch as, in spite of the extensive retinal hæmorrhages, the veins were small, not large and tortuous as is usual. This caused a very reasonable doubt as to the diagnosis. The case shows well the interaction of pathological states of the two sides of the intraocular vascular system, an interaction which should never be forgotten in considering the results of disease of the one or the other. It is most probable that the first lesion in this instance was the localised nodule of endarteritis at the lamina cribrosa. In consequence of this the intraocular circulation would be slowed, and thrombosis of the central vein in the usual situation would be favoured. This would cause the profuse retinal hæmorrhages. But

the heightened blood-pressure caused by the venous obstruction would evidently react unfavourably on the endarteritis, which would increase. Hence the arterial supply would be more and more interfered with until, when the lumen of the artery became quite filled up, it would be entirely cut off. The engorged veins would practically cease to be filled from the arterial side, while they would be drained to a certain extent by the small collaterals about the nerve head, and they would therefore become small and empty again. In addition, some of them were destroyed by thrombosis and organisation. I have already reported an instance of obliteration of the artery in a case of thrombosis of the central vein (Case 4 of my former paper), and I have also recorded a case in which there was reason to believe that the vein had become thrombosed secondarily to an obstruction of the artery.* Without doubt such cases have caused much confusion in the literature, and have led to the statement that intense hæmorrhagic retinitis may be due to disease confined to the arterial side of the circulation, a statement which, if true, would only lead to accumulated difficulties, and which I believe to be entirely erroneous. Harms has also reported similar cases, and comes to the same conclusion. The disease of the arteries is the indirect cause of the thrombosis of the central vein, but it is the thrombosis of the vein which is the cause of the clinical picture.

The case shows some points of resemblance to Cases 6 and 7 reported above, viz., the comparatively early age of the patient (34), and the occurrence of retinitis proliferans, and of a new-formed membrane on the anterior surface of the iris.

CASE 11.—*Thrombosis of the left central vein of two months' duration in a man, aged* 78. *Iritis. Glaucoma about nine days later. No improvement with treatment. Enucleation* $4\frac{1}{2}$ *months from onset of symptoms. Organising thrombus in*

* R. L. O. H. Rep., vol. xvi, pt. iii, Case 2, p. 227.

central vein some distance behind the lamina cribrosa. Corneo-iridic angle more occluded on the temporal than on the nasal side.

I am indebted to Mr. R. W. Doyne for the material and notes of this case:—

A man, aged 78, came to the Oxford Eye Hospital on December 20, 1904, complaining of failure of vision of the left eye of two months' duration. There had been no pain. The iris was discoloured, inactive, and bound down by a broad synechia below. V.R. with + 1·5 sph., 6/9. V.L. fingers at 12 inches. Tension of left perhaps slightly higher than that of right. With the ophthalmoscope, thrombosis of the central vein was diagnosed by Mr. Menteith Ogilvie. Nine days later the tension of the left was distinctly raised (+ 1), and the cornea hazy. *The anterior chamber was very deep.* The eye remained painful and injected. The pupillary edge became vascularised, and on January 26, 1905, a large hyphæma occurred. Signs of iritis with severe pain continued, the tension remained continuously high, and the eye was therefore excised on March 8, 1905.

The eye was bisected by Mr. Doyne, and the half of it containing the central vessels was sent to me for examination.

Pathological Examination.

The eye has been divided horizontally. The anterior chamber is of average depth; its angles seem to be occluded. The lens is *in situ*. The vitreous is absent. The retina is studded with hæmorrhages. The disc is not cupped.

Microscopical Examination—

Optic Nerve and Central Vessels.—The nerve entrance was accidentally cut longitudinally, a direction not well suited to the exact study of changes in the vessels and of their relations to one another. In the present instance, however, the obstruction happened to be found, and the case is reported as giving a good general view of a thrombus, and as furnishing a useful commentary on the cases already described.

The veins on the papilla are large and filled with normal blood corpuscles. They have normal walls. As the vessel is

passing through the lamina cribrosa the blood within it gives place to homogeneous coagulum, in which a few polymorphonuclear leucocytes are present (Plate VII, Fig. 18, A). Some distance behind the lamina other cells appear in the coagulum, with somewhat elongated pale nuclei; these form a knot, which for a short distance fully fills the lumen of the vein (B). It then begins to taper off and ends in a sharp point free within the lumen. A few blood corpuscles are present in the space between this conical mass and the vein wall. No collateral vessel is seen to enter the vein at the point where the obstruction ends, but, owing to the direction of section, one may easily have been overlooked. The vein remains perfectly patent from the point of obstruction to the cut surface of the nerve. There is nowhere any inflammatory infiltration of the surrounding connective tissues. The artery is normal throughout, the nerve is atrophic, and there is no glaucomatous cupping.

The cornea is normal. The iris is very atrophic and its root is firmly adherent to the back of the cornea on both sides, but much more extensively on the temporal. The measurements are—temporally, 1·60 mm.; nasally, 0·64 mm. The ciliary muscle is atrophic and flat, and the choroid is also atrophic. Both the retinal arteries and veins are thick walled, the process being one of fibrosis. Hæmorrhages are abundant, but usually not very large. The outer nuclear layer is best preserved; all layers internal to it are much scattered and destroyed; the nerve fibre and ganglion cell layers especially are very highly atrophic.

The case is useful, as showing in a single section points which have to be reconstructed from a series when the nerve is cut in the usual manner. It will be evident that a transverse section through the lamina cribrosa would give an appearance similar to Fig. 7 of my former paper; a section through the cellular knot would be similar to Figs. 3, 5, 7, 14, or 17 of the present paper; and one through the conical projection, to Fig. 6 of the former paper.

Remarks.

It may be useful to go over some of the points mentioned in my former paper, to see how far they should be modified in view of the larger material now at disposal. It would seem that the collection of more fully examined cases has tended to simplify the questions at issue. The cases given in this paper are not in any way picked, but include every instance in which a diagnosis of thrombosis of the central vein was made with the opthalmoscope, or, if the fundus had never been seen, by macroscopic inspection of the divided eye. In every one of them an obstruction was found in the vein which fully accounted for the symptoms. Harms also found an obstruction in the vein in every case in which he examined the whole course of it in transverse serial sections. Sidler Huguenin's and Baquis' are also cases in point. There can hardly be a doubt, therefore, that in all typical cases an obstruction would be found in some part of the central vein. If this be admitted, it at once clears away two of the six explanations which, as I stated in my former paper, have been advanced to explain the clinical picture, namely, (1) *multiple emboli or thrombi of the retinal arteries* and (2) *changes in the retinal vessels* (*hyalin thickening, endarteritis, and endophlebitis*) *not the result of either thrombosis or embolism.* Another explanation, *hæmorrhage into the substance of the nerve*, has never met with any proof since it was propounded by Deutschmann, and may probably be safely given up. *Multiple thrombi in the retinal, without thrombosis of the central vein* must be admitted to be theoretically possible, but it has so far not been shown to occur in a case in which the whole course of the vein was properly examined, though believed by Harms to be present in one of his cases in which the nerve was cut longitudinally. On the other hand, extensive thrombosis of the retinal veins has been found associated with proved thrombosis of the central vein. The former possibility must therefore be

accepted with all reserve until more definite proof is forthcoming.

Of all the explanations given, only two seem to have stood the test. *Primary disease of the vein wall* seems to have been clearly proved in one of Harms' cases and in Case 8 above. In the vast majority of cases, however, the lesion is a *thrombus* in a more or less advanced condition of organisation. This was found in 14 out of 16 of my own cases, and in 6 out of 7 of Harms', in which the obstruction was found with certainty. It may seem a small thing to be able to say that the clinical condition known as "thrombosis of the central vein" is indeed due to a thrombus in that vessel, but anyone who has read the recent literature of the subject will not consider it so.

While admitting that there are many gaps in our knowledge, an attempt may be made to sketch the pathological history of a case of thrombosis. There is a certain amount of evidence that the cause of thrombosis in the central vein may fall under one of two headings. In one set of cases there is no inflammation of the vein wall either at the point of thrombosis or elsewhere. Such cases usually occur in old people with extensive endarteritis of the central artery or its retinal branches. The thrombosis in this case is probably due chiefly to slowing of the current, assisted no doubt by some degenerative senile change in the endothelium of the vein. Exceptional instances of primary disease of the vein wall would fall under this class. Nephritis and possibly syphilis would be powerful predisposing causes, but are by no means necessarily, or even frequently, present. In the other class there is widespread round-cell infiltration of the vein wall, both in the nerve and in the retina. Such cases tend to occur in younger people, and there is often a history of some general disease, such as gout, rheumatism, syphilis, sepsis, or influenza (see Cases 6 and 7). In my own experience a history of influenza is frequently given. Such cases are, perhaps, specially liable to the occurrence of retinitis proliferans. The second class probably furnishes most of

the patients who remain in good health years after the attack; those included in the first class will be liable to various accidents. While, however, it is possible to cite typical cases in each class, it is doubtful how far they are practically separable in every instance, and at any rate they will not be mutually exclusive. When thrombosis has occurred there seems to be no difference in the prognosis with regard to the eye in the two classes.

Whether due to slowing of the current or to primary inflammation of the wall, the thrombosis is always deposited within or immediately behind the lamina cribrosa. I have discussed the reason for this in former papers. The first reaction on the part of the tissues seems to be a proliferation of the endothelium, which invades the clot from all sides (Figs. 1 and 16). Some authors hold that all the subsequent stages of organisation in small vessels, such as the central vein, proceed from this proliferated endothelium, but I believe the evidence rather favours the participation of the surrounding tissues. The comparatively small, darkly-stained, elongated cells which are found in cases with fairly advanced organisation, the indefiniteness of the outer boundaries of the cellular knot, and the total loss of the normal outline of the vein wall (Figs. 9, 11, 13), are all points in favour of organisation from the surrounding tissues, not from the endothelium of the vessel.

The subsequent steps vary in different cases. Most commonly the vein becomes greatly shrunken from the contraction of the organising tissue within it, and finally it may totally disappear over a certain area. In other rarer instances the organising material becomes canalised, new endothelium-lined channels burrow into it from the old lumen, and a considerable circulation may be restored. In any case the vein does not remain obliterated for more than a short distance. The thrombus only extends as far as the nearest collateral branch; if this happens to be large, a full lumen is restored at once, if small, this only occurs gradually from the entrance of other collateral branches. If a

sufficiently long piece of nerve has been excised, the lumen will always be found to be restored before the point of exit of the vein.

It is easy to understand why the retinal hæmorrhages and enlargement of vessels follow occlusion of the central vein. The occurrence of glaucoma is a much more difficult problem. I have already discussed this subject in my former paper, and have little to add. The present series fully confirms the statement, that even in early cases vitreous hæmorrhages are not present. In recent cases also the corneo-iridic angle is already found occluded, but often only slightly, and the extent of the adhesion bears a rough relation to the duration of the glaucoma. I still consider the most probable explanation to be the more albuminous nature of fluids the of the vitreous, and therefore of the aqueous, due to the venous obstruction and retinal hæmorrhages behind. But this explanation is not altogether satisfactory, for it does not easily account for the occlusion of the angle by *adhesion* of the iris to the back of the cornea—an adhesion around which there are no inflammatory infiltrates in recent cases. In the somewhat similar case of serous iritis, where the increased tension, when present, is probably also due to an alteration of the fluids to be drained off, the angles are not usually found occluded by adhesion. On the whole, therefore, it must be confessed that a fully satisfactory hypothesis has not yet been advanced to account for the glaucoma. It is hardly conceivable that it is due to the damming back of the small quantity of lymph which normally leaves the eye by the posterior perivascular lymph sheaths.

It is apparently not due to the carrying forward of the lens and iris, since, as has been repeatedly mentioned, the anterior chamber is usually of normal depth, or at least much less shallow than in primary glaucoma. In this point there is a certain agreement with serous iritis, except that in the latter the anterior chamber is not merely normal, but is increased in depth. I have already shown the clinical importance of this depth of the anterior chamber. When

there is a history of loss of vision without pain, and when pain and glaucomatous symptoms have come on subsequently, the other eye remaining normal and with a full field, the diagnosis probably lies between thrombosis of the central vein and intraocular tumour, provided that the glaucoma is not obviously secondary to iritis, etc. If now the anterior chamber is found to be of normal depth, the probabilities are in favour of thrombosis of the central vein, if shallow, in favour of intraocular growth. Unfortunately the value of the distinction is somewhat lessened by the fact that if glaucoma has ensued on thrombosis of the central vein, it is nearly as hopeless to save the eye as in the case of a tumour, but at least the case is not so urgent, and the attempt may be made. The measurements given in the pathological examinations seem to show that the lens is not unduly large in these cases.

I have several times pointed out the curious fact that in cases of glaucoma following upon thrombosis, the corneo-iridic angle is often much more widely occluded on the temporal than on the nasal side. In 11 cases in which the globe was bisected horizontally this was found 9 times. In one of those in which it was not found an iridectomy had been performed. The greater occlusion on the temporal than on the nasal side does not seem to be due to any anatomical difference, as I was unable to detect any in a normal globe; in especial there was no difference in the average thickness of the ciliary body or height of the ciliary processes in a number of serial sections taken through the middle of the pupil. In order to find whether or not this is the rule in other forms of glaucoma, I examined some other glaucomatous eyes. Unfortunately it is the custom, where no reason to the contrary exists, to divide globes sagitally. Moreover, in many of those divided horizontally the glaucoma was secondary to wounds, and was therefore not strictly comparable with that under consideration. It is also unusual to obtain other forms of glaucoma in an early stage and uninterfered with by opera-

tion. I was therefore only able to find six which were suitable for purposes of comparison. In four of these the angle was equally occluded on both sides (two cases of sarcoma of the choroid, one of buphthalmia, one of old injury). In one the angle was slightly more occluded on the nasal than on the temporal side (case of ? primary glaucoma in a diabetic), and in one slightly more on the temporal than on the nasal (old primary glaucoma). It is possible therefore that this is a peculiarity of the glaucoma following upon hæmorrhagic retinitis, but as I am unable to offer the least explanation of it, I must be content to simply record the observation, leaving its explanation to future research.

I have endeavoured to obtain particulars as to the subsequent course of thrombosis cases. For this purpose I have made use of the cases already published by me, those cases reported in the present paper (except three, which are too recent to be of value), and some cases from the practice of the hospital, all of which I have personally observed at one period or another. For the use of the notes of the latter I am indebted to Mr. Treacher Collins and to Mr. Percy Flemming.

This gives a material of 20 cases. Of these I have been unable to trace eight. Of the remaining 12 two died; Case 1 of my previous paper died in hospital of nephritis; Case 2, as Mr. Snell has kindly informed me, died suddenly, probably from cerebral apoplexy, four and a-half months after the first onset of symptoms. Before his death he had had severe headache and some mental symptoms, but no further attacks of loss of consciousness, etc., as described in the previous report. Another (Case 1 of the present paper) was in the last stages of chronic Bright's disease in March, 1906.

The following interesting history was obtained in a case seen five years previously:—A woman, aged 54, came to the hospital under Mr. Treacher Collins in April, 1901. She

had thrombosis of the right central vein. The urine contained no albumen or sugar. The day after she left hospital, according to a statement made by her husband, she had a "fit" and was unconscious for a whole day. She was an invalid for three or four months afterwards, but subsequently recovered sufficiently to go about fairly freely. During the ensuing two and a-half years she had occasional similar attacks of less severity. Two years ago she had a severe attack, and on recovering consciousness had right hemiplegia. This has never been fully recovered from, but it has not increased, although she has had several subsequent fits of unconsciousness. Her general health during the whole period has been fairly good. The vision of the right eye has remained practically unaltered since her first visit, that of the left has never been affected. This history would seem to point to thrombosis of cerebral vessels, the hemiplegia being due to thrombosis of the vessels supplying the internal capsule. This case, and the case of Mr. Snell, are the only instances which I have personally met with of cerebral symptoms associated with thrombosis of the central vein.

Another case was seen five years after thrombosis had been diagnosed. It concerned a woman aged 45, who was under the care of Mr. Treacher Collins in March, 1901. Thrombosis of the right central vein had been present probably for five weeks. There was no albumen or sugar in the urine. When seen in March, 1906, the veins were still very tortuous, but not enlarged. They were rather small and extremely sclerosed. The arteries were also small and accompanied with white lines. There were no hæmorrhages, but many large white patches all over the fundus, especially one extremely large and slightly raised patch upwards and inwards; in this patch there were some small curly new-formed vessels. Small nets had formed round the periphery of the disc, and its edges were hazy. The vision of this eye was 1/60, and it had not altered in the five years. The vision of the left was 6/6,

and with +2 D sph., J. 1. The left fundus was perfectly normal. Her general health had been good throughout the whole period. The tension was normal in both eyes.

The following case was watched for two and a half years. A woman, aged 42, was under the care of Mr. Treacher Collins in November, 1903. She had typical thrombosis of the central vein of the left eye. The urine contained no albumen or sugar. Her subsequent visits were irregular, but nine months later she came with the vitreous full of hæmorrhage. Two months later this had largely cleared up, and an exquisite retinitis proliferans was revealed, with much sclerosis of the retinal vessels. She was seen occasionally during the next 18 months. The retinitis proliferans altered very little, the connective tissue becoming rather more transparent, and allowing the vessels to be more clearly seen. The right eye remained normal throughout, except for a moderate degree of arteriosclerosis. The tension of both was normal. Her general health continued unimpaired.

In another case under the care of Mr. Flemming the fundus altered very little in two years. The veins remained very large and tortuous, white degenerative patches gradually appeared, and small nets formed in the periphery of the disc. No fresh hæmorrhages occurred; the other eye was healthy except for some arteriosclerosis; the tension of both was normal, and his general health had remained good. In this case there was a very faint trace of albumen in the urine on two different occasions. His peripheral arteries were also rigid, and his pulse of high tension.

Another case showed no alteration in four months, and a year later his medical attendant, Dr. A. K. Thomson, mentions nothing of an affection of the other eye, or of glaucoma in the diseased eye, in a note which he kindly sent me as to his condition. The urine contained a trace of albumen in this case, and the peripheral arteries were very rigid. He suffered much from bronchitis.

In the case in which expulsive hæmorrhage followed

upon iridectomy (Case 8) Mr. Flemming informs me that in March, 1906, there were no hæmorrhages in the other eye; the disc was pale, and both arteries and veins small. The urine contained no albumen or sugar.

A case of thrombosis of the superior temporal vein was watched for three and a half years, during which hæmorrhage occurred into the vitreous several times, but neither glaucoma nor retinitis proliferans ensued. This case could not be traced in March, 1906.

Two other patients were not seen, but wrote to say that they were in good health, and that the other eye had remained unaffected.

From a consideration of these cases the most important fact which emerges is the total immunity of the other eye. I have not personally seen or heard of a case in which it became affected, and the literature is almost equally silent on the subject. With the doubtful exception of v. Graefe, who wrote before this class of cases was well separated from other conditions of retinal hæmorrhage, and of Goh,* whose case was exceptional in many respects, no author seems to mention affection of the other eye. This is rather an unexpected fact in a condition which might be thought to depend chiefly on general angiosclerosis. It is, however, of great importance, since the patient may be assured almost with certainty that his remaining eye is safe.

The figures do not show in what proportion glaucoma follows upon thrombosis of the central vein, since the clinical cases in which glaucoma *did not* ensue were all gathered from two cliniques, whereas the pathological material in which it *did* ensue was collected from the whole practice of the hospital, as well as from private sources. The collection within a period of about three years of 16 cases in which glaucoma ensued, sufficiently shows that there must be some definite connection between

* In Goh's case hæmorrhages occurred in both eyes a few days before death from septic poisoning. A thrombus was found in the right central vein, not in the left (Arch. f. Ophth., vol. xlviii, pt. i, p. 147, 1897).

the two conditions. Indeed, it may be said that in any given case there is very considerable danger of the occurrence of glaucoma. It is, however, evident from the cases quoted above, that the condition may last for a period of years, and may be complicated with vitreous hæmorrhage *without* giving rise to glaucoma. One important clinical lesson to be drawn from this fact of a liability to glaucoma, is that, when a diagnosis of thrombosis has been made, no mydriatic should ever subsequently be employed—not even homatropine. In four out of 16 cases in which glaucoma followed, there were the strongest reasons to believe that it was directly precipitated by the use of a mydriatic (atropine twice, homatropine twice). In one of these it developed immediately, while the patient was waiting for ophthalmoscopic examination.

It does not appear from the above data that the occurrence of thrombosis gives much help in forming a prognosis as to the life of the patient. The prognosis does not seem to depend so much on the thrombosis *per se* as on the general health of the patient. Two of the cases died, but one of them had advanced Bright's disease, while the other had had an attack of apoplexy. Another case, which was *in extremis* when last heard of, was also the subject of advanced Bright's disease when first seen. In all these cases a bad prognosis would have been given quite independently of the thrombosis. On the other hand, we have cases watched for 5, $3\frac{1}{2}$, $2\frac{1}{2}$, $1\frac{1}{3}$, $1\frac{1}{4}$ years, without the least deterioration of their general health. In only two cases did symptoms of thrombosis elsewhere (in the brain) ensue. The numbers are, however, too few, and the cases are not yet sufficiently long under observation to allow of any very certain conclusion being drawn.

Description of Plates IV to VII, Figs. 1 to 18.

In all the photographs in which both vessels are shown the vein is above.

Fig. 1. × 120.—Central vein in anterior part of the lamina cribrosa in Case 1. It is obstructed by a mass which shows a reticular structure. No red corpuscles could be seen in it, but it contains polymorphonuclear leucocytes, and also larger paler cells, possibly derived from the endothelium. The original outline of the vein is distinct, and the mass has shrunk away from the wall. There is no round-cell infiltration of the surrounding tissues. The thrombosis is evidently not of long duration.

Fig. 2. × 120.—Termination of the thrombus immediately central to the lamina cribrosa in the same case. The lumen is restored by the accession of a large branch from the surrounding connective tissues. From this point onwards the lumen of the vein was normal.

Fig. 3. × 120.—The central vessels in Case 2. The lumen of the central vein (above) is greatly encroached upon by a cellular organised tissue, with a distinctly fibrous ground substance. The original vein wall can no longer be traced with certainty. From the appearance of this section alone it would be difficult to say whether the obstruction was due to endothelial proliferation or an organised thrombus, but the examination of the whole series made the latter more probable. A few sections farther up the nerve the vein became completely occluded for a short distance. The artery is normal and filled with blood.

Fig. 4. × 120.—Method of restoration of the lumen in the same case. The general form of the vein is restored, and its endothelium is present. The lumen is mostly filled with coagulum. Into this a collateral branch from the surrounding connective tissues plunges, carrying with it a stream of normal red blood corpuscles. From this point backwards the vein was normal, and its lumen contained blood.

Fig. 5. × 120.—The central vessels from Case 3. The vein contains a thrombus, in which the process of organisation is more advanced than in the last instance. The ground substance is more definitely fibrous, and the mass is more cellular and shrunken. It has shrunk away from the surrounding connective tissues—probably artificially. It is situated at the posterior level of the lamina cribrosa. The artery is somewhat collapsed, but shows no endarteritis. In this case only a short piece of nerve was excised with the globe, and the vein had not recovered a lumen before it reached the cut end of the nerve.

Fig. 6. × 170.—A retinal vein from the same case. It is occluded by a completely organised thrombus. There is a considerable collection of pigment granules (blood pigment) round it. Note the comparatively good preservation of the outer nuclear layer, with almost total atrophy of the layers internal to it.

Fig. 7. × 120.—The central vessels in Case 4. The position of the vein is shown by the letter A. This section is towards the posterior level

of the lamina cribrosa. A short distance further forward the shrinkage of the vein was still more extreme. In the section shown there is a small shrunken coagulum in which a few red corpuscles could be seen with higher powers. There is a distinct round-cell infiltration of the surrounding connective tissues at one side. The artery is obliquely cut at this level, and does not show well the changes described in the text.

FIG. 8. × 120. The central vessels from Case 5. The section shown is from the anterior part of the lamina cribrosa. The outline of the vein is distinct, but its lumen is occluded by an almost homogeneous mass, in which a few leucocytes and other cells are present. In the artery the elastic membrane has separated from the media, presumably artificially. Within it there is a mass of detritus formed by the breaking down of the large vacuolated cells (see also Fig. 10 and description of Case 4 in the text). Within this again there is a single layer of endothelium resting on a kind of basement membrane. The lumen is exceedingly small and eccentrically placed. The appearances are probably not due to proliferation of the endothelium, which remains as a single layer lining the lumen, but to proliferation of the cells of the normally very thin layer of subendothelial tissue lying between the endothelium and the elastica.

FIG. 9. × 120.—Section still within the lamina cribrosa from the same case. The vein is entirely obliterated, its position being marked only by a more cellular knot in which the nuclei are mostly oval (A). The artery shows the same changes as in the last figure. Note the density of the connective tissue around the central vessels as compared with the next figure. This is always found at the lamina cribrosa, and may have some importance in determining the frequency of vascular disease there.

FIG. 10. × 120.—Section from the same case further back. A small lumen has been restored in the vein, but its walls are extremely thick and infiltrated. The artery shows better than in the preceding photograph the cellular character of the tissue from which the detritus found more anteriorly is formed. Some of these cells are very large and contain more than one nucleus—resemble, in fact, small giant cells. The single-layered unaltered endothelium is well seen.

FIG. 11. × 120.—The central vessels from Case 6. The section is from the posterior part of the lamina cribrosa. The lumen of the vein is encroached upon from one side by a conical mass. There is much round-cell infiltration both in the mass and in the surrounding connective tissues on the side from which it springs. Nearer the surface of the papilla the vein was completely obliterated, and its position indistinguishable; further up the nerve its lumen was speedily restored. The artery is somewhat obliquely cut, but has normal walls.

FIG. 12. × 120.—A retinal vein from the same case, showing an unusual amount of round-cell infiltration in its wall. This, and the thrombus in the central vein were probably associated with an attack of influenza, during which the sight of the eye was lost.

FIG. 13. × 120.—The central vessels in Case 7. The section is from the posterior part of the lamina. A normal and patent vein was present in front of this level. The outline of the vessel cannot be traced. Its position is occupied by an area of highly cellular tissue, in which three small lumina are present, each lined with endothelium and containing homogeneous coagulum, but no corpuscles. In the section immediately in front of this level the same cellular tissue was present but without the lumina. The condition probably represents an early and incomplete stage of canalisation. The obstruction of the vein is only present over a very small area. The lumen was restored a few sections up the nerve and remained patent.

FIG. 14. × 120.—The central vessels in Case 8. The level of the section is immediately posterior to the lamina. The vein is completely occluded by a loose cellular mass, somewhat similar to that shown in Fig. 1, but rather more advanced in organisation. There is no surrounding round-cell infiltration. The artery has normal walls, and is filled with blood.

FIG. 15. × 120.—The central vessels in Case 9. The section is from a point somewhat behind the posterior surface of the lamina. The obstruction in the vein differs from that shown in previous figures in having a definite concentric arrangement both of its fibres and nuclei. There is also a small central lumen containing coagulum and blood. In sections farther up the nerve this was still more reduced in size so as to be of practically capillary dimensions. The mass has shrunk away from the wall—probably artificially. The case is probably one of endothelial proliferation. The artery is normal, and contains a little coagulum.

FIG. 16. × 120.—The central vessels in Case 10. The section is within the lamina cribrosa. The vein is of full size and somewhat enlarged. Its lumen is occupied by granular detritus, in which a few broken-down red corpuscles are visible. There is also a delicate reticulum with some large, pale, probably endothelial, cells in its meshes. The artery is much shrunken and completely occluded by endarteritis.

FIG. 17. × 120 —A section behind the lamina from the same case. The vein is much smaller, but still not greatly shrunken. It is occupied by a fully organised mass of tissue. There is no surrounding cell infiltration. The lumen of the artery has become patent. It is only slightly narrowed by endarteritis at one side. The endothelium is preserved.

FIG. 18. × 120.—A longitudinal section through the nerve in Case 11. From the region of the lamina cribrosa (A) backwards the vein is occupied by a homogeneous coagulum. There is slight endothelial proliferation. Some distance behind the lamina (B) the coagulum becomes invaded by cells—polymorphonuclear leucocytes and larger paler cells. The obstruction ends in a pointed extremity, which is free in the centre of the lumen. The vein wall is normal above this point, and there is nowhere any round-cell infiltration of the surrounding tissues. The artery is not present in this section.

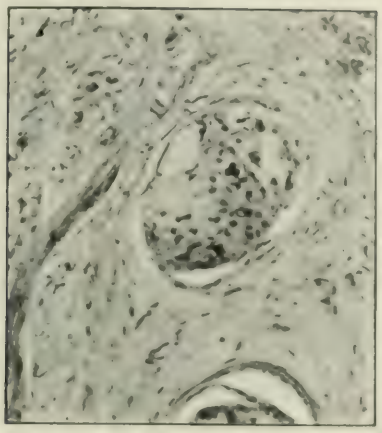
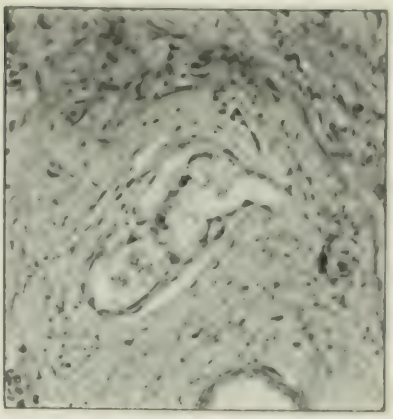


FIG. 1.



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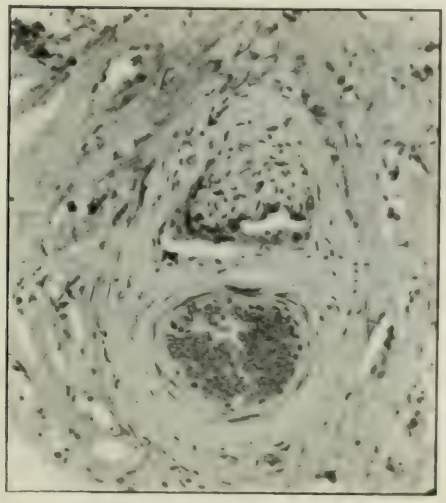

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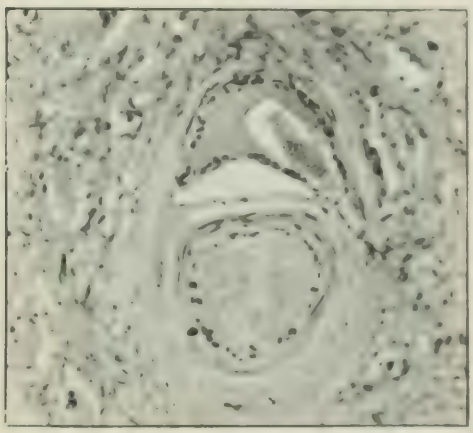

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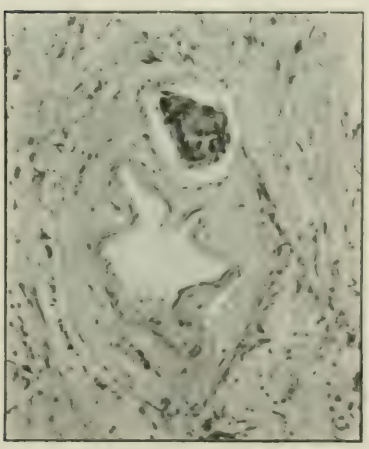

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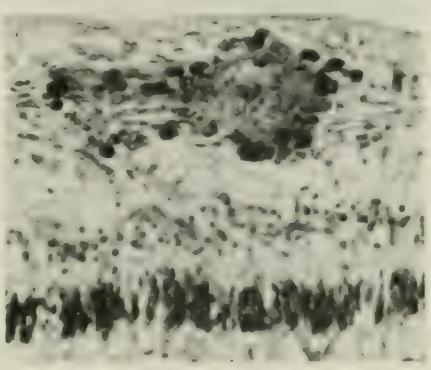

FIG. 6.

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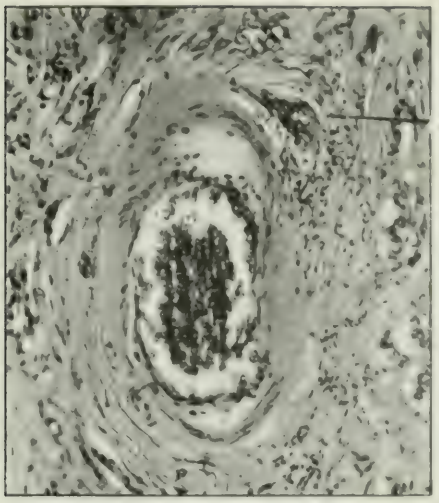

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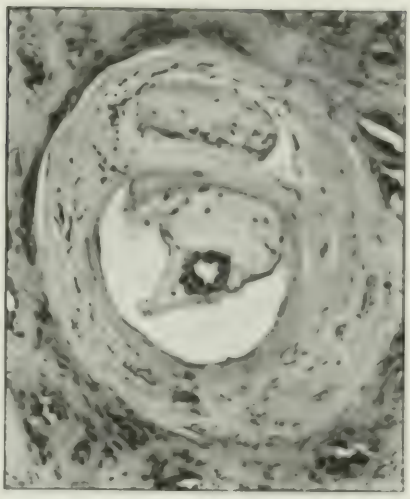
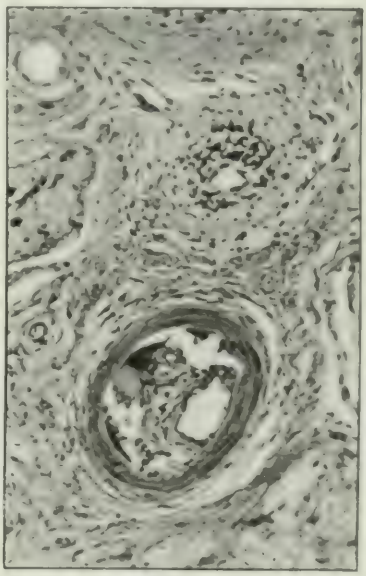


FIG. 8.

FIG. 9.



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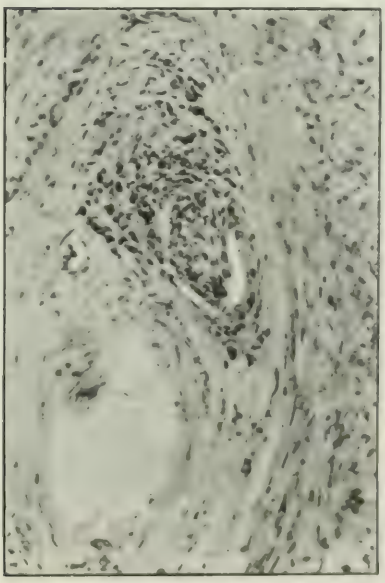

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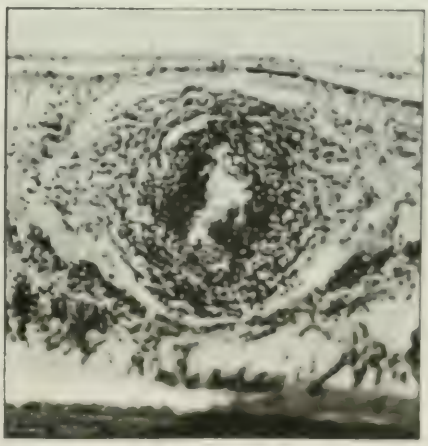

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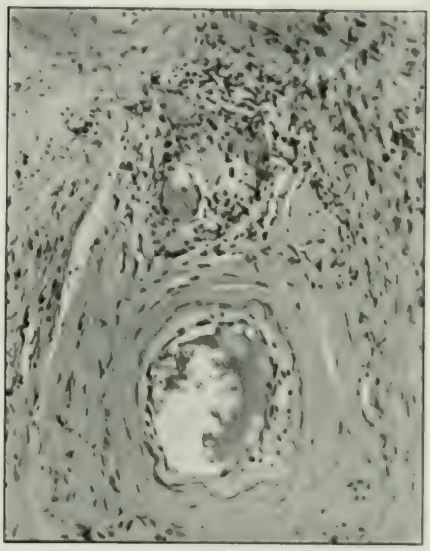

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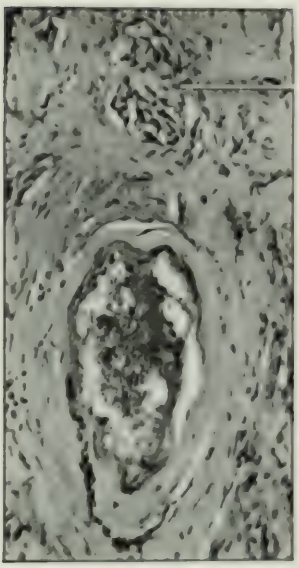

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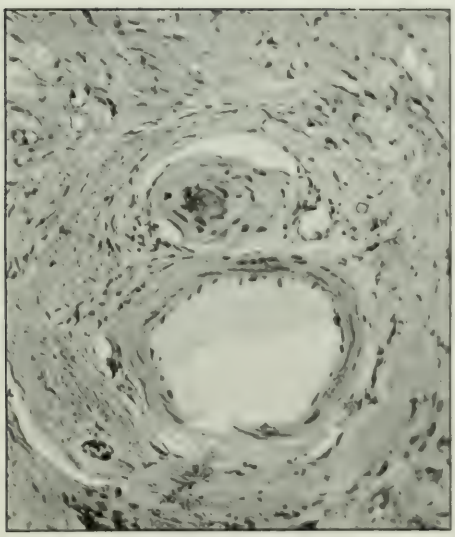

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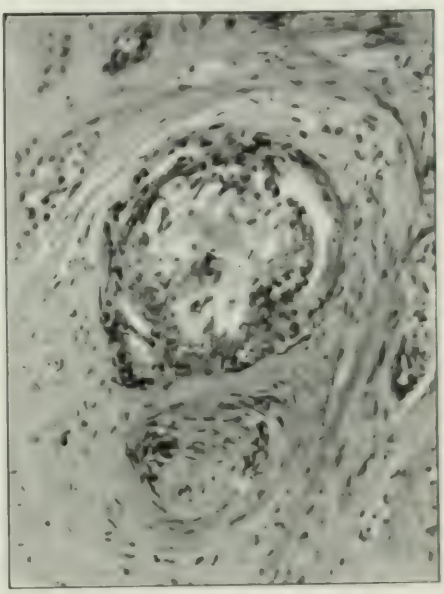

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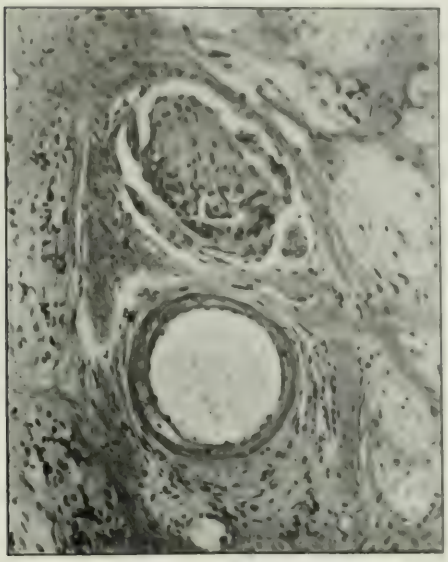

FIG. 17.

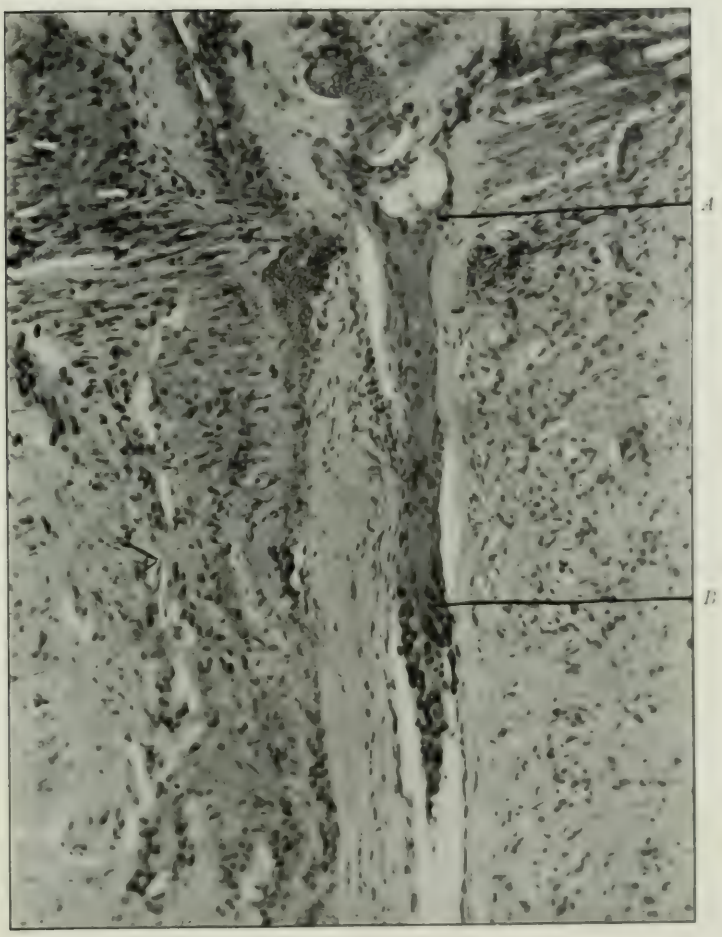

FIG. 18.

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ON METASTATIC INFECTION OF THE EYE ASSOCIATED WITH (*a*) CEREBRO-SPINAL MENINGITIS; (*b*) TYPHOID FEVER.

From the Andrew Clark Laboratories, London Hospital.)

By M. S. Mayou.

Cases of definite endogenous infection of the globe are comparatively rare. The two cases described below show very well the early and late stages of the disease. The first case, which was associated with cerebro-spinal meningitis, was of 24 hours' duration, whilst the second had lasted several days. In both cases the specific micro-organism was found in the globe in the pure state.

(*a*) Cases of endogenous infection of the eye associated with cerebro-spinal meningitis which have been previously reported, have all been cases in which the disease in the eye had lasted for some time, and had led to the condition known as pseudo-glioma. Further, in those cases which have been recorded by Cross [1], Nettleship [2], Collins [3], Stephenson [4], Flemming [5], and Axenfeld [6], the specific micro-organism was not demonstrated in the globe: the inflammatory process was said to have travelled to the globe *viâ* the optic nerve and sheath, those structures being found to be inflamed. In the case about to be described the infection of the eye was undoubtedly metastatic.

Case 1.—A. L., male, æt. 3. Admitted to the London Hospital, under Dr. Head, November 1, 1905; died November 3.

History of the Onset.—Had been ill only since the morning. Did not take food well the day before, but ran about as usual. In afternoon complained of being tired. Restless all night. At 5.30 A.M. kept crying for water and was very hot. Went to doctor in the morning and was given medicine. Sick once after

first dose. Had not known mother since breakfast. Much screaming. Had much shaking in the arms. A fixed look in the eyes.

Previous Health.—Very good. One other child alive. One died of "twisted gut." No one else ill in the house.

Condition on Admission.—The fontanelles were still patent. Heart *nil.* Lungs clear. Abdomen *nil.* Child lay on back or preferably (apparently) on right side. Eyes half open and staring. Slight rigidity of the neck, with retraction. Took no notice of lights or moving objects. Did not blink when hand was moved in front of the eyes suddenly. Frequently put hands up to head as though in pain; mostly, perhaps, the right hand to right ear. Occasionally there was a coarse shiver or clonic spasm of the arms, which always came on if child was roused. He screamed if disturbed at all, and was rather irritable, but appeared unconscious of what was going on around him. The lower limbs were somewhat spastic. There was no discharge from ears, and never had been any. No rash. No coryza. Tonsils large, no membrane.

Ears: Right drum: malleus red, drum somewhat indrawn, no bulging. Left drum: normal, rather indrawn.

Eyes: Discs clear. Pupils large when child was roused, equal, and reacted. Fundi, well marked retinal reflex.

November 2.—Child had a restless night. Temperature steadily rose until, at 8 A.M., it was 104°. Pulse ran up to 160, and respiration to 58. The child suffered frequently from "shaking fits"; both hands were affected, but the right mostly. Left hand, (?) paresis. During the night the child kept putting the right hand up to the right ear and side of head.

Eyes: Slight divergent squint at times; eyes moved asymmetrically. Right pupil was smaller than left, but they often varied. Fundi clear. Vessels seemed large.

Ears: Left drum had a whitish plaque in the centre, just below handle of malleus, and was indrawn. Punctured, no fluid whatever in middle ear.

Breathing rapid, no difficulty. Tonsils very large, red, inflamed, no membrane. Tongue very thickly furred. No rash. Fontanelle pulsating.

November 3.—Left lung a little dull, crepitations and râles,

(?) pneumonia. Respirations and pulse very rapid. Temperature, 104°. Child worse. Sweating. Not so cyanosed.

Eyes.—Large hypopyon was present in the right eye at 8.15 A.M., which had developed during the night. No red reflex was obtained. Anterior surface of lens covered with lymph. Eye a little congested. No wound of cornea or other part of eye.

More râles in the chest. Hypostatic œdema and collapse. Right lung most affected, left to some extent.

At 2.30 patient was very ill and obviously dying. Respirations had become slow. Pulse very rapid and weak. Cyanosis less marked, giving way to a dusky pallor. Right eye as before. No red reflex in spite of dilatation by homatropine. Left pupil dilated. Vessels quite clear. Veins rather large and congested. Disc clear (seen five minutes before death). No further signs. Died 2.45 P.M.

Post-mortem.—Body weight, 20 lbs. 8 ozs. Much P.M. staining, back, neck, and thighs. Hypopyon, right anterior chamber.

Pleuræ: No fluid, no adhesions.

Lungs: Surface mottled, showing areas of collapse in upper lobes. Lower lobes deep red in colour, slightly aërated, exuded fluid on pressure. Pieces did not sink in water.

Larynx: Healthy. Bronchi and trachea injected throughout. Heart: 3 ozs.; left ventricle firmly contracted. Right ventricle contained white clot. Ventricles not contracted. Muscles soft, deep red. All valves quite healthy.

Vessels: Healthy.

Abdomen: Stomach and intestines healthy. Peyer's patches slightly congested. Appendix healthy. No excess of fluid.

Spleen: 2½ ozs. Deep red, capsule smooth. Soft. Malpighian corpuscles prominent.

Right kidney: 2½ ozs. Pale, smooth, capsule stripped readily. Demarcation good. No diminution of cortex, which was striated with parallel lines of injected vessels.

Left kidney: Suprarenal vessels healthy.

Genito-urinary system: Bladder healthy.

Liver: 1 lb. 5 ozs. Pale, smooth, not soft. Healthy. Gall bladder full of bile.

Alimentary canal: healthy.

Brain: 3 lbs. The surface of the brain was redder than usual,

owing to congestion of vessels. The sulci contained a small amount of thin yellow pus lying in arachnoid space. Smears showed *Diplococcus meningitidis* in small numbers. No excess of fluid in ventricles and substance of brain, and on section appeared normal.

Spinal cord : Had lost its translucent appearance and looked somewhat greenish. The dura was coated with a thin layer of exudation which could be scraped off. The nerve roots were matted as they passed out through the membrane.

Right eye : Was removed and reserved for further examination. The optic nerve appeared normal to the naked eye.

Ears : No pus in middle ears.

The eye was hardened in formol and divided horizontally. The optic nerve, having been previously removed, was cut transversely in serial section.

The *retina* and *optic nerve* were normal. There was no distension of the nerve sheath or swelling of the nerve head.

The *vitreous* was clear except near the lens, where it was slightly cloudy.

The *lens* was in its normal position and there was no evidence of any injury to any part of the globe.

The *anterior chamber* contained a considerable amount of pus, shrunken and adherent to the back of the cornea, iris, and anterior capsule of the lens. Smear preparations of the pus showed enormous numbers of diplococci which were not stained by Gram's method, and were similar in appearance to those found on the surface of the meninges ; unfortunately no culture could be made, as the specimen had been placed in formol, but they were evidently the *Diplococcus meningitidis*. The organisms were so numerous in the smear as to appear more like a culture preparation than pus from the body.

The eye was embedded in celloidin and paraffin, and the optic nerve, which had been previously removed, was cut transversely in paraffin. The optic nerve and central vessels were normal, there was no leucocytosis into it or its sheath, and no organisms could be found in sections stained with methylene blue.

The *retina*, *choroid*, and vessels were normal as far forward as the ora serrata.

The *lens* was normal. Around the *ciliary body* and entangled in the suspensory ligament of the lens and also in the region of the ora serrata was a large exudation of polymorphonuclear leucocytes. These pus cells were also found in the anterior chamber, especially at the lower angle. They were also found adherent to Descemet's membrane in the other parts of the cornea. The central and upper parts of the substantia propria were free from polymorphonuclear leucocytes, but below in the region of the Canal of Schlemm, and spreading inwards on the outer surface of Descemet's membrane, were a number of these cells.

The *iris* in its upper part was free from leucocytes, and there was no evidence of post. synechiæ. Below, near the angle, the iris was packed with polymorphonuclear cells.

The condition, therefore, is one of very early panophthalmitis starting in the ciliary region. Considerable controversy has arisen as to whether the infection of the globe in these cases is due to the direct extension of the inflammation down the nerve sheath or to embolic infection. In this case, in which the fundus was seen immediately before the onset of infection, and death took place within 24 hours after the fundus was examined, the posterior part of the globe, nerve and nerve sheath were found to be perfectly healthy on microscopic examination; we have, therefore, positive proof that the infection did not take place by direct spreading from the meninges, and therefore infection must have taken place through the blood stream. The exact situation of the embolus was not discovered, but was evidently in the ciliary body, since polymorphonuclear leucocytes were most numerous in that region. The infiltration of pus cells in the neighbourhood of the Canal of Schlemm is of interest in that, as will be seen in the second case, a ring ulcer formed in that situation which subsequently caused necrosis of the cornea.

(*b*) Judging by the literature, cases of panophthalmitis in typhoid fever seem very rare, but perhaps this is owing to their not being reported, since they were noted as early as

1826, but at that date the differential diagnosis between typhus and typhoid fever had not been established.

A case, starting in a similar manner to the one about to be described, is reported by de Schweinitz [7], the only difference being that in his case there had been no previous inflammation in the eye.

Case 2.—H. R., male, æt. 22; an engineer's fitter. Attended the out-patients' department of Moorfields Hospital on June 20, 1899, under Mr. Tweedy, with double iridocyclitis. He attended again on October 6, 1899, when he was admitted as an in-patient. The following was his condition at the time of admission:—He was a strong, healthy man, and had previously been in the Navy. There was no history of syphilis or other trouble. Urine, Sp. G. 1028, no albumen or sugar; his temperature was 99°. He was suffering from double iridocyclitis.

L. eye. The fundus could be seen, and there was a small retinal hæmorrhage. V. 6/60 Tn.

R. eye. Chronic iritis with partly occluded pupil; some retinal hæmorrhage. T + 1. Bare P. of L.

On October 16, paracentesis on the right eye was performed, that is to say, ten days after admission. The same day his temperature rose to 104°, and some crepitations were heard at the bases of both lungs. Two days previous to this he had complained of severe headache. The right eye was much improved; there was slight ciliary injection, the anterior chamber was deep, the wound healed well, and there was no pain.

As his general condition did not improve, on October 21 he was transferred to the London Hospital under Sir Stephen Mackenzie. On admission his temperature was 103° to 106°; pulse 140, sordes of mouth, few râles in chest, and pains in the left side of the abdomen. The spleen was enlarged, typhoid spots were present, and Vidal's reaction was positive. On October 25 some œdema of the right conjunctiva was noticed, which rapidly increased during the next three days. There was no note of any hypopyon. The patient did not complain of any pain.

On October 29, under chloroform, the right eye was excised by Mr. Roxburgh with much difficulty and considerable

hæmorrhage. The patient made a good recovery from the operation. On November 8 a quantity of fluid was withdrawn from the left pleura. Subsequently the patient made a good recovery and remains well up to the present time, the sight of the left eye being in much the same condition as when he attended Moorfields.

Histological Examination.—The globe was hardened in formol and bisected horizontally.

The anterior chamber was filled with a tough fibrinous exudation, the root of the iris being pushed forward against the posterior surface of the cornea, occluding the angle of the chamber. The anterior chamber contained comparatively few pus cells.

The *lens* and *suspensory ligament* were intact.

The *vitreous* chamber was filled with reddish-brown pus. Smear preparations of the contents showed a large number of bacilli staining with methylene blue, but not by Gram's method, and although cultures could not be made owing to the specimen having been immersed in formol, the organism was probably the *Bacillus typhosus.*

The pus had made its way through the choroid about the equator, and through the sclera, just behind the insertion of the internal rectus muscle, forming an abscess beneath it.

The *cornea* was necrotic. The epithelium had disappeared from the surface. The substantia propria in the centre was comparatively free from pus cells, whilst round the margin a ring ulcer had formed which, towards the outer side, had caused complete perforation of the cornea, but on the inner side Descemet's membrane was still intact. (The early stages of this condition are well seen in Case 1.)

The *iris* and *ciliary body* were infiltrated with pus cells.

The *retina* had completely disappeared.

The *choroidal vessels* in the posterior part of the globe were converted into large venous sinuses which were enormously engorged with blood, whilst anteriorly the choroid was thin and atrophic ; equatorially in some situations it had disappeared altogether.

The facts that the wound from the paracentesis had

healed perfectly before there were any signs of inflammation, which clinically did not start in the anterior part of the eye; that the inflammation did not come till nine days after the operation, and that the vitreous chamber was full of pus, whilst the anterior chamber was comparatively free and only contained the fibrous membrane as the result of the old exudation, indicate that the infection must have taken place from within. The fact that a bacillus having the same characteristics as the *Bacillus typhosus* was found, together with the fact that the patient had other metastatic symptoms, *e.g.*, pleurisy, make it practically certain that the case was one of endogenous infection due to the *Bacillus typhosus* grafted on to an old chronic cyclitis of unknown origin.

For the use of the notes on the first case I am indebted to Mr. Lister and Dr. Head; for the notes of the second case to Mr. Tweedy, Mr. Roxburgh, and Sir Stephen Mackenzie; for the photographs of the micro-organisms to Mr. Henderson, and to Mr. Coats for the use of the Moorfields Hospital camera.

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Description of Plates VIII and IX, Figs. 1 to 4.

Fig. 1.—Smear preparation of the pus from the anterior chamber of Case 1, showing the *Diplococcus meningitidis*. Stain—carbol-fuchsin. (Photo, E. E. Henderson.)

Fig. 2.—The lower angle of the anterior chamber (Case 1) showing the polymorphonuclear leucocytes in the iris and angle of the chamber. Note also the exudation in the neighbourhood of the canal of Schlemm

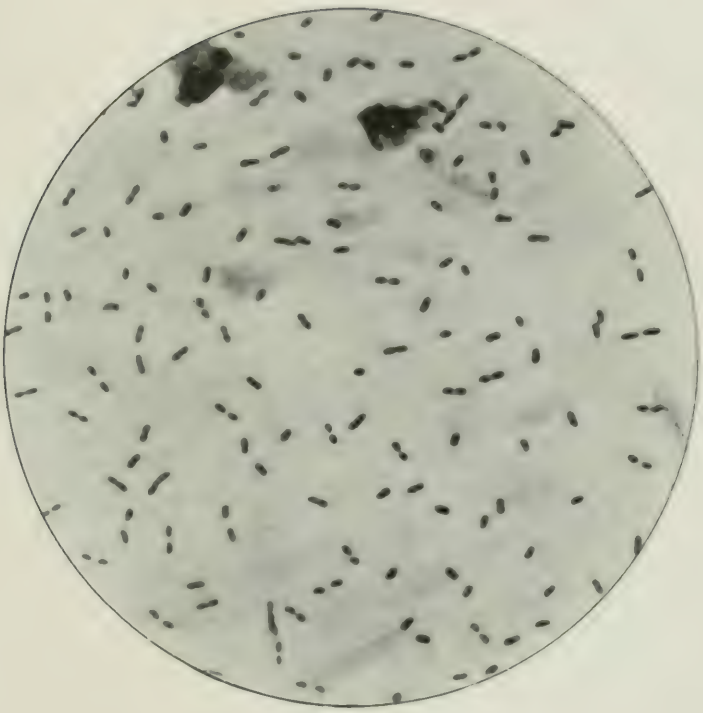

FIG. 1.

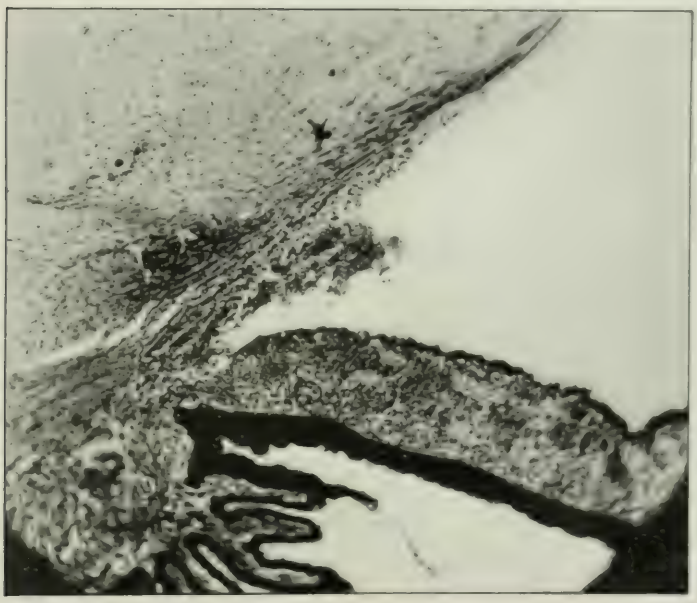

FIG. 2.

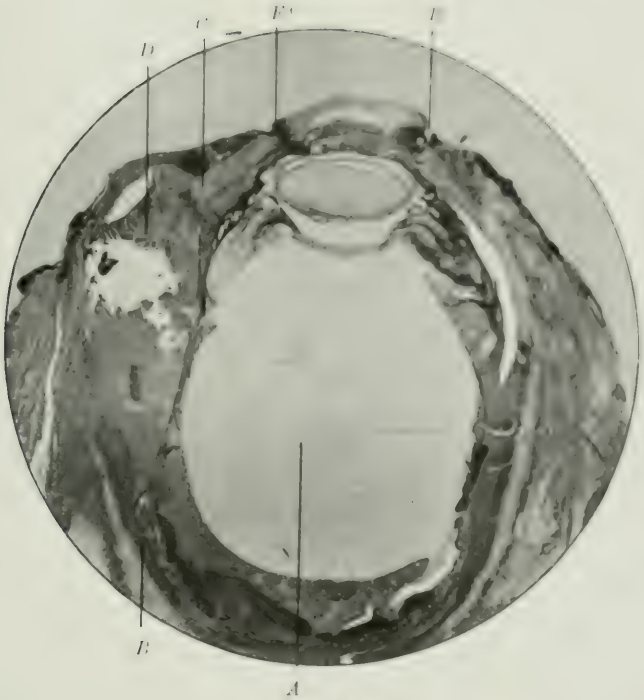

FIG. 3.

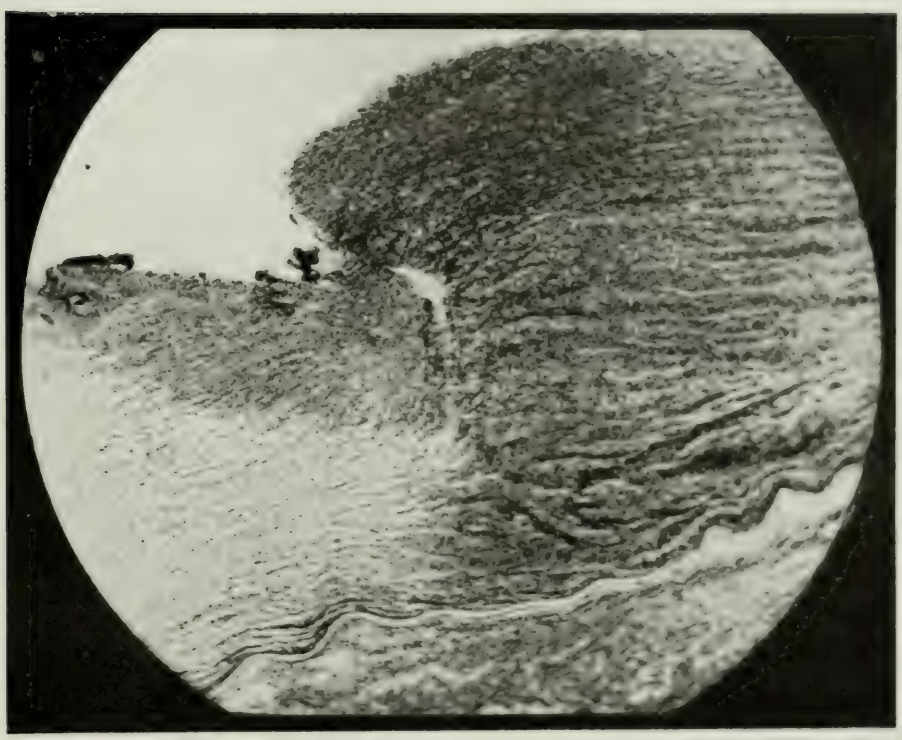

FIG. 4.

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(early stage of the condition seen in Fig. 4). In the region of the ora serrata there was also a large collection of pus cells. The posterior part of the globe and the optic nerve were normal.

FIG. 3.—Horizontal section through the globe (Case 2). (A) The whole vitreous chamber was filled with pus, but is not shown in the section owing to the shrinkage brought about by the alcohol. (B) The choroidal vessels are enormously dilated at the posterior pole. The pus has ruptured through the choroid and sclerotic (C), and has formed an abscess beneath the tendon of the internal rectus (D). The anterior chamber is filled with old fibrinous exudate, in which there are comparatively few pus cells (E, E′). The ring ulcer which has formed round the cornea was perforated on the outer side.

FIG. 4.—Section through the ring ulcer towards the inner side (E′, Fig. 3) showing the necrotic cornea comparatively free from leucocytes. Descemet's membrane is still intact.

RETINA IN GLAUCOMA CUP.

By Malcolm Langton Hepburn, F.R.C.S.

To find retina or retinal elements in a glaucoma cup is extremely rare, and the cases described by Kampherstein [6] and Parsons [8] are probably unique. The question, therefore, naturally suggests itself as to how it came to be situated in this position.

I am inclined to regard it merely as a final stage in a series of changes produced in certain eyes which eventually become the subjects of glaucoma.

Although portions of retina are not often found actually inside a glaucoma cup, yet to find pathologically the excavation filled in with fibrous tissue is by no means so uncommon. Several cases have been described by Schnabel [1], Axenfeld [2], Krukenberg [3], Gama Pinto [5], Ginsberg [7], and Roscher [4], and I have collected together 30 similar cases from the pathological records of the hospital during the last four years; and it is the subsequent behaviour of this fibrous tissue which determines the character of the contents of the glaucoma cup.

There has been a good deal of discussion amongst the various writers, not only as to the origin of the contents of the cup, but also as to whether the glaucoma or the fibrous tissue existed first; and the cases have sometimes been described as "Glaucomatous excavation of the lamina cribrosa without excavation of the Optic Nerve." The explanation given by Axenfeld [2] and Krukenberg [3] is that some severe inflammatory condition of the papilla was present first and the glaucoma followed later. Other theories put forward by Krukenberg are that either there was a congenital excavation of the lamina cribrosa, into which some subsequent infiltration entered, or that a papillary neuritis takes place at the bottom of an old glaucomatous cup. Roscher [4], Gama Pinto, and

Ginsberg [7] favour the latter view; but the clinical evidence is not very convincing, since Roscher's case is that of a woman, aged 25, who had suffered from what was probably interstitial keratitis 10 years before, a history which hardly encourages a theory of primary glaucoma. To me it seems unlikely that an acute neuritis should take place in structures which have actually been atrophic for a long time, though Schnabel describes a case of optic neuritis, developing in an old glaucomatous eye, as a result of cerebral tumour. In a certain number of cases passive exudation does take place into a pre-existing glaucoma cup, probably as a result of acute inflammation of the ciliary body; and under these circumstances it is conceivable that subsequent organisation and contraction of the fibrous tissue might draw down some portions of retina near the cup; but by far the larger majority of the eyes examined are the subjects of secondary glaucoma, that is, secondary to some injury, operation, or inflammatory condition involving the cornea, iris, and ciliary body, thus leading to long-standing iridocyclitis, the evidences of which have always been found pathologically.

According to the extent and duration of these inflammatory processes, so we find various changes produced in the different structures, and the combined influence of chronic inflammation and degeneration produces such conditions as folded retina (Paton [10] and Parsons [11]), hyaline degeneration, retinal degeneration, etc., which are often most marked near the optic disc. Moreover, the formation and proliferation of fibrous tissue in the neighbourhood of the disc in connection with the central blood vessels, where there is most mesoblastic tissue (Parsons [9]), is commonly met with clinically, and in an extreme form as retinitis proliferans; but if these changes occur simultaneously with the inflammation elsewhere, strands of connective tissue spread out in the form of wings and attach themselves ultimately to surrounding structures, as shown in Figs. 1 (A) and 2 (D). Kampherstein also suggests the formation of fibrous tissue as a result of proliferation rather than of organised exudate.

Sooner or later an attack of glaucoma comes on, evidenced by pain and increased tension. The thrusting back of the lamina cribrosa produces stretching out of the fibrous tissue formed on the disc, and large spaces may result, as shown in Figs. 1 (B) and Fig. 3, which are very likely to become filled with blood or hyaline material. In other cases the fibrous attachment to the lamina cribrosa and surrounding structures is so firm that the parts adjacent to the disc are dragged upon, and thus we find degenerated retina, folded retina, etc., eventually settled in the excavation. In Parsons' case, a large mass of fibrous tissue on one side of the glaucoma cup indicates how the retina has been dragged over, and many of the specimens I have collected show the pulling on the retina in the earlier stages.

In the majority of cases, however, the retina does not hold, and we get the appearance seen in Fig. 4, where the retinal tissue is only united by a very fine strand (C), which would probably soon have given way, leaving a free end with its base attached to the bottom of the cup, Fig. 3 (D); quite a large number of cases can be seen in which this has occurred. I am very much indebted to Mr. Coats for his assistance in taking photographs of the sections, and for giving me every facility in getting the specimens together.

In the accompanying list of cases there are 30 in which definite fibrous tissue appears in the glaucomatous excavation, and out of this collection Nos. 12, 22, 30, and 32 represent Figs. 1, 2, 3, and 4 respectively. It has not always been possible to determine in each case when the glaucoma first appeared, as the date of onset has not always been recorded, but I have considered the occurrence of severe pain as indicative of the commencement of increased tension.

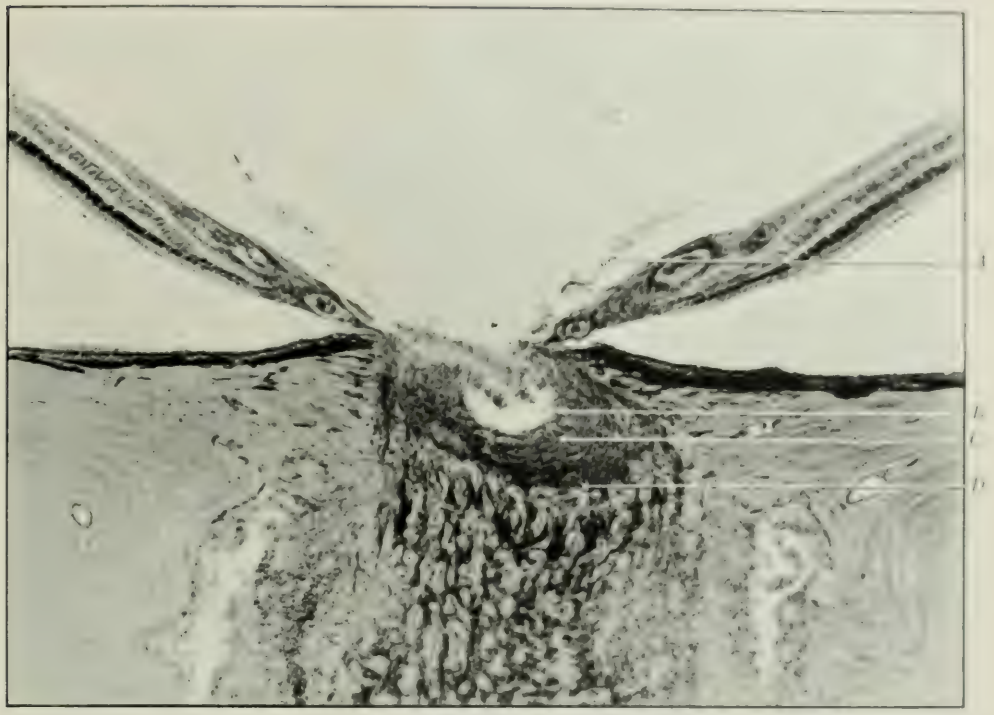

FIG. 1.

FIG. 2

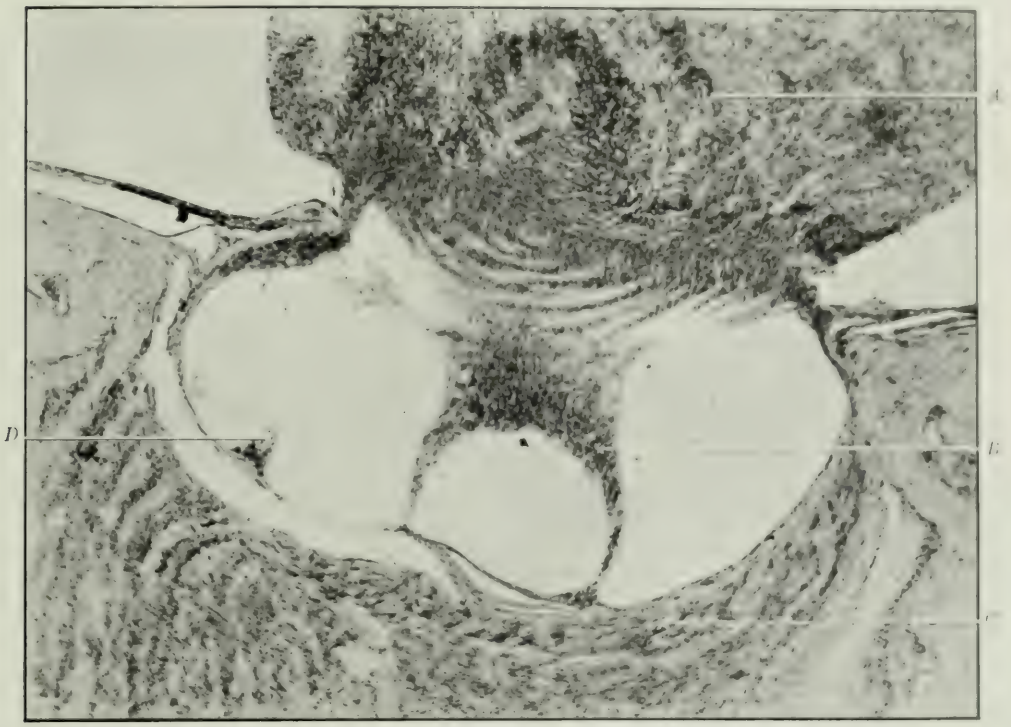

FIG. 3.

FIG. 4.

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Description of Plates X and XI, Figs. 1 to 4.

Fig. 1.—A case of iridocyclitis of doubtful duration, followed by secondary glaucoma. The cup is full of fibrous tissue (C) stretching out over the surface of the retina in the form of wings (A). The connective tissue in the cup is in an early stage of stretching, and a space is being formed in the centre of the mass (B). Lamina cribrosa is situated at D.

Fig. 2.—A similar case to that shown in Fig. 1, the inflammation having probably extended over a period of nearly 20 years. The mass (B) filling the glaucoma cup sends wings over the retina on each side (A), and at one part it shows an attachment to the degenerated retina (D), thus indicating an early stage in the process of dragging down. Lamina cribrosa is shown at C.

Fig. 3.—A section of a glaucoma cup from an eye which had been struck with a stone 19 years before removal, causing a detachment of the retina. The fibrous tissue formed in the cup is attached loosely to the degenerated retina above (A), and has become so stretched that large spaces have resulted. These spaces often contain blood or coagulated material. D. Piece of fibrous tissue lying free. C. Lamina cribrosa.

Fig. 4.—A section of the glaucoma cup from an eye which was struck by a boot 4 years before removal. In this case the retina has been dragged down almost into the cup, but just below the edge the uniting strand is in the act of giving way, unable to withstand the pull which the receding cup has put upon it.

A. Retina.
B. Stretched retinal tissue.
C. Fibrous band.
D. Lamina cribrosa.

Name.	Age.	Surgeon.	Eye.	History.
(1) J. W.	4	Mr. Lang. Dec. 2, 1901.	L.	Ophthalm ianeonatorum. Eye inflamed ever since.
(2) Jessie R. ...	68	Mr. Spicer. Jan. 22, 1902.	L.	Two years ago injury. Attended R. L. O. H. ever since.
(3) George P. ...	60	Mr. Lawford. Feb. 8, 1902.	L.	O. P. since 1897.
(4) Wm. F. ...	50	Mr. Gunn. Mar. 29, 1902.	L.	O. P. 11.12.01. Had left inflamed 3 weeks previously.
(5) Elizabeth D. ...	66	Mr. Silcock. June 10, 1902.	R.	19.11.01. R. Idy. much inflamed. 10.2.02. Accidentally rubbed. Never well since.
(6) Eliza J., ...	68	Mr. Lawford. June 11, 1902.	R.	Sight of right failed slowly in a few months. Blind 12 months.
(7) Edmund M. ...	75	Mr. Lang. June 16, 1902.	R.	Feb., 1902. R. became inflamed after a fall.
(8) Maria J. ...	69	Mr. Lawford. June 21, 1902.	L.	In 1905. L. extraction; 7 months later a needling.
(9) Frances C. ...	70	Mr. Gunn. July 23, 1902.	L.	4.11.99. L. Idy. 24.1.00. L. extraction. 12.1.01. L. needling. L. eye never comfortable since needling.
(10) Fk. K. ...	61	Mr. Lang. Nov. 12, 1902.	L.	Fifteen weeks ago kick from a horse. Operation 3 weeks ago.
(11) Mary D. ...	58	Mr. Spicer. Nov. 15, 1902.	L.	28.6.99. O. P. with chronic glaucoma. Blind 1½ years ago.
(12) Mary W. ...	61	Mr. Silcock. Dec. 13, 1902.	L.	Twenty years ago inflammation in left (?). At this time an Idy. performed in right.
(13) Emily S. ...	30	Mr. Gunn. Dec. 20, 1902.	R.	7.4.97. R. extraction. 5.7.97. R. needling. Capsule got adherent to wound. 7.7.97. Idy. to relieve tension.
(14) Sarah S. ...	70	Mr. Gunn. Dec. 24, 1902.	L.	Left eye "bad" for 18 years.

Clinical condition.	Onset of glaucoma.	Pathological examination.
tercalary staphyloma and iritis.	... ...	Retina degenerated. Fibrous tissue in cup.
tis and iridocyclitis.	Increased tension off and on for 18 months.	Arteriosclerosis. O. D. cupped, and full of fibrous tissue.
tensive choroiditis. Round patch ust above disc, which appears illed in.	Painful and increased tension 9 months.	Retina very atrophic, two calcareous masses near the disc. Much nuclear connective tissue in cup.
nnus, iritis.	Painful and increased tension for 3 months.	New fibrous tissue in the optic cup.
is caught up in wound. Vesicular keratitis. Some fine K. P.	?	Vessels atheromatous. Small amount of fibrous tissue in cup.
robably a case of chronic glaucoma.	Painful and increased tension for 4—5 weeks.	Cup filled with new fibrous tissue.
flammation for 2 months, producing iritis with post-synechiæ.	?	Small amount of fibrous tissue in cup.
epeated attacks of iridocyclitis.	Had pain in left probably for some time, but no note as to how long.	Cystoid cicatrix. O. D. full of fibrous tissue.
vidences of iridocyclitis. K. P. Vitreous opacities.	?	*No* cup, but retina heaped up and folded near the disc.
lging scar at upper sclero-corneal nargin. Iris adherent. Dislocated lens.	Tension was +3 when removed.	Retina degenerated. Fibrous tissue lining optic cup.
me K. P. Evidence of old iritis.	Glaucoma (chronic for 3 years).	Optic cup filled with fibrous tissue, which sends wings out over the retina.
Sympathetic ophthalmia; evidence of iridocyclitis; fine K. P. in left.	?	Optic cup filled with fibrous tissue, which sends wings out over the retina.
me iris got caught up in wound, with resulting inflammatory reaction.	Pain and tension for 3 weeks, but some tension 4 years ago.	Optic cup full of fibrous tissue containing leucocytes.
eratitis. Old iritis with synechiæ.	Blind 3 months.	Optic cup full of fibrous tissue, which contains dilated spaces.

Name.	Age.	Surgeon.	Eye.	
(15) Letitia G. ...	50	Mr. Lang. Feb. 23, 1903.	R.	
(16) John F. ...	60	Mr. Flemming. Mar. 7, 1903.	L.	Eight weel stone.
(17) Jas. P. ...	28	Mr. Lawford. Mar. 14, 1903.	L.	Said to be l ago, blow since.
(18) James W. ...	70	Mr. Gunn. Mar. 28, 1903.	L.	Thirty yea years ago
(19) Mary B. ...	75	Mr. Silcock. Apr. 21, 1903.	L.	Twelve or
(20) Jas. D. ...	40	Mr. Gunn. Apr. 22, 1903.	R.	17.12.98. July, 1902 lowed by
(21) Ellen C. ...	33	Mr. Lang. Apr. 30, 1903.	R.	Injured by
(22) Caroline R. ...	55	Mr. Morton. May 5, 1903.	R.	Left eye fir ago L. f operated
(23) Maud E. ...	17	Mr. Marshall. Nov. 27, 1903.	L.	Ten years a to see sinc
(24) Ellen W. ...	53	Mr. Silcock. Feb. 16, 1904.	R.	Five years get dim; in 1903, w
(25) Bessie B. ...	37	Mr. Spicer. Feb. 18, 1904.	L.	"Was bad" mation. champagn detached
(26) Annie B. ...	65	Mr. Fisher.	R.	Four years

Clinical condition.	Onset of glaucoma.	Pathological
Myopia. Patches of choroiditis. Evidence of chronic iritis.	?	Optic cup filled which contai blood.
Keratitis. Iritis. Iris bombé.	?	Much fibrous t
Iridocyclitis.	Painful for 15 hours.	Not much fibr but folded near disc.
Ulceration of cornea. Hypopyon. T. +. No P. L.	Blind for 3 years.	Fibrous tissue tended to forr
Large corneal scar with iris adherent.	Pain. Blind for 1 month.	Small amount optic cup.
Evidences of old iritis. T. + 1. No P. L.	Sight began to fail 5 months ago. Blind for 2 months.	Optic cup fi retina.*
Keratectasia, calcareous band of cornea. Iritis. No. P. L.	Painful for 3 weeks.	Optic cup cont of fibrous tiss
? Sympathetic. Evidence of iridocyclitis. Much K. P.	... ...	Optic cup full sending wings
Buphthalmic. Corneal nebulæ.	Painful for 3 weeks.	Choroido-retin contains small tissue.
Much acute inflammation. Iris adherent to corneal wound. T. +3. No P. L.	... ...	Optic cup con trated fibrous
Corneal ulcer. Bombé iris. T. +2. No P. L.	Three months painful.	Retina detached Optic cup fille tissue, sendin membrane ove
Hypopyon ulcer.	... ...	Optic cup fill

Name.	Age.	Surgeon.	Eye.	History.
(28) Emily B. ...	52	Mr. Collins. Oct. 24, 1904.	R.	Six months ago eye was red and painful; then worse 1 month ago.
(29) Emma M. ...	38	Mr. Lang. Feb. 27, 1905.	R.	Always divergent, and amblyopic. Inflammation 1½ years, and again 6 months ago.
(30) John R. ...	55	Mr. Lawford. May 27, 1905.	L.	Gradual failure of sight in left eye for 9 years without pain or tenderness.
(31) John M. ...	77	Mr. Lang. June 9, 1905.	R.	Struck by a boot 4 years ago. 2½ years ago went blind gradually without pain.
(32) Thos. R. ...	58	Mr. Spicer. Aug. 11, 1905.	R.	Ten years ago struck by stone, followed by detachment of retina.

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Clinical condition.	Onset of glaucoma.	Pathological examination.
T. + 3. No P. L.	?	Retina shows haemorrhages. Optic cup partly filled with fibrous tissue.
Bullous and filamentous keratitis. Bombé iris. T. + 2. No P. L.	Painful for several months.	Retina degenerated, and shows much new-formed connective tissue. Retina attached by strand to bottom of glaucoma cup.
Cornea hazy; no A. C. Iris attached to back of cornea. Lens shrunken and opaque. No P. L. T. + 2.	Red and painful for 4—5 weeks.	Atrophic iris wholly adherent to cornea. Leucocytes in vitreous. Optic cup contains fibrous tissue stretched to form spaces which are full of blood.
Transverse band of corneal opacity. Lens dislocated and opaque. T. + 3. No P. L.	Painful for 2 months.	Iris bound down and infiltrated; ciliary body also infiltrated. Fibrous tissue in optic cup stretched to form spaces.
Large irregular staphyloma of sclerotic in equatorial region. T. + 1.	?	Retina detached and folded. Attached by strand to bottom of optic cup.

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